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POLYPOID DISEASE OF THE COLON

A PROPOSED SURGICAL PROCEDURE IN SELECTED CASES

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IN RECENT years the literature on polyps of the colon has become extensive. Interest has been stimulated in this rather rare disease because of the increasing frequency with which the lesions are found, due to modern methods of examining the colon. Also, the striking tendency of these tumors to undergo malignant changes has been the basis of interest in many of the pathologic reports. However, comparatively little has been learned and the knowledge of this disease remains much as it was in 1916 when Murphy[50] said: "The etiology of intestinal polypi—like the common wart—is shrouded in mystery; whence they come, why they go, is like the riddle of the Sphinx."

TERMS

Much confusion appears in the literature regarding the terminology of polyps of the colon.[68] Terms appear such as polyposis, multiple polyposis,[2, 47, 66] multiple adenomas,[27, 34, 59, 61] polyposis intestini,[65] polypoidosis,[5] polypoid disease, disseminated polyposis.[70] Hence, it is often difficult to ascertain the type of pathology under discussion. The term used by one writer in describing polyps, limited to an anatomic segment, may be used by another in describing a colon entirely lined with polyps. Also, pathologic terms are freely intermingled with clinical terms which adds to the difficulty.

A polyp is a growth from a mucous membrane, either pedunculated or sessile, made up of hypertrophied mucous membrane, or it may be a true tumor. When there is more than one, they are, of course, multiple. Hence, multiple polyps may mean two polyps located in the colon or thousands of polyps studding the entire large bowel. Buie[6] has clarified

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the nomenclature of this disease by calling any condition in which two or more polyps are present in the colon multiple polypoid disease. To this term he appends the segment of colon involved to describe the condition. Thus, when only the sigmoid contains polyps, the condition is known as multiple polypoid disease of the sigmoid. When the entire colon is lined with polyps, it is known as multiple polypoid disease of the entire colon. The use of these terms is clear and simple and they will be used throughout this paper.

CLASSIFICATION

Polyps of the colon include any tumor which projects into the lumen of the bowel. Any of the tissue elements forming the component parts of the bowel wall are capable of such growths. Hence, hemangiomas, fibromas, lipomas, myomas, and adenomas may be considered under the term polyp. However, only the adenomas, which are more numerous than all of the other varieties combined, offer exceptional interest to the surgeon and pathologist.

Erdmann and Morris[25] have classified these tumors into: (1) adult (acquired) type, (2) adolescent (congenital, disseminated) type. This classification, although used most frequently in the literature, is of limited value in many cases. By this grouping polyps develop after birth (acquired type), or there is a factor present prior to birth which predisposes to the formation of polyps (congenital type). This classification leaves much to be desired when one attempts to study the origin, age incidence, segmental distribution, and necropsy findings in this disease of the colon.

Bargen and Comfort[4] classified multiple polyps from the standpoint of origin as follows: (1) preexisting inflammatory disease (colitis), (2) arising as innumerable polypoid projections without inflammation, (3) few disseminated adenomatous growths discovered at autopsy.

Excellent histologic studies of polyps of the colon have been made by Schmieden and Westhues,[63] Fitzgibbon,[30, 31] David,[15] Dukes,[24] and others. The conclusions of Schmieden and Westhues are similar to Fitzgibbon's. They classify polyps into three groups. In Group I the polyps are usually solitary and long, covered with normal epithelium. The stalk is made up of loose connective tissue. There is no branching of the villi. These polyps are benign. In Group II there are changes in both the epithelium and connective tissue. The epithelium has bulk and the cells are compressed from side-to-side, producing multilayered buds. The nuclei are elongated and take a deep stain. The villi are branched and there are papilla-like projections into the lumina of the glands. These polyps are potentially malignant. In Group III the structural changes are more exaggerated than in Group II. There is great proliferation of the epithelium. The arrangement of the cells is distinctly irregular. This proliferation is out of proportion to the growth of the underlying

connective tissue. Hence, the growth is downward, extending into the muscularis mucosa. This type is the most malignant.

Duke[24] believes that the pedunculated types are not as dangerous as the sessile types, but that on the cap of pedunculated polyps malignant changes may occur. He points out that in the sessile variety the pathologic characteristics are the branching of the villi, the bowing upward of the muscularis mucosa with the formation of a catarrhal collar around the periphery, and in the clefts between the primary and secondary tumors. These cells, he states, are the ones that undergo malignancy.

RELATIONSHIP TO MALIGNANCY

Nowhere, according to Ewing,[26] can be demonstrated more clearly the logical transition from simple inflammatory hyperplasia to tumors which are morphologically, pathologically, and clinically adenomas and carcinomas.

Coffey (quoted by Graham[34]) says: "There is probably no benign process in which there is a higher incidence of malignancy than colonic polyposis." Lockhart-Mummery states: "Almost all recorded cases of multiple polypi of the colon eventually become malignant."

Hullsiek,[38] in an analysis of 127 cases of multiple polyposis, found the incidence of carcinoma to be 36.4 per cent. Soper,[64] in 61 cases, discovered malignancy in 26, or 43 per cent. In a study of 166 colons containing polyps, Lawrence[42] found 19 cases, or 11.4 per cent, to have existing malignancy.

Many[54, 65] believe that most carcinomas of the colon have their origin in polyps. Rankin[56] says: "I believe that it is a reasonable conclusion that a great many carcinomas of the colon, perhaps more than we suspect, are thus etiologically explainable. The commonest sites of polyps and carcinoma of the lower end of the gastrointestinal tract are the sigmoid and rectum. The ratio of eight cancers of the sigmoid and rectum to one in the rest of the colon is maintained in the incidence of polyps."

ETIOLOGY

Although a great deal of study has been given to this disease, the etiology remains obscure. In the acquired type the polypoid formation (pseudopolyposis)[73] is, undoubtedly, a hyperplastic response to inflammation. Polypoid growths in the colon, secondary to ulcerative colitis, are relatively common. Bargen and Comfort[4] found 69 such cases in 693 patients suffering from ulcerative colitis. They state that "of five cases of multiple polyposis, four will be on the basis of ulcerative colitis." Amebiasis,[1] bacillary dysentery, and other infections[41, 62] of the colon have also been reported as the primary causes of these growths.

The etiology of the adolescent (congenital) type has been the basis of much interest. The tendency of this disease to occur in families was rec-

ognized by Cripps[14] in 1882. Since then many familial cases have been reported.[36, 49, 52, 72] Hullsiek[37] obtained a positive family history in 11 per cent of 127 cases. Dukes,[23] Lockhart-Mummery, McKenney,[47] and others have experienced the difficulties and the tremendous tasks involved in rounding up the members of families to ascertain the frequency of polyps. Lockhart-Mummery[43] believes that the disease is transmitted as a Mendelian dominant. He says that "a change, or mutation, has taken place in the genes of some individual who has not personally exhibited the diseased condition, but who has passed the mutated genes on to his descendants."

The most striking tendencies of this disease to occur in families have been in cases reported in which the entire colon contained polyps. This familial tendency is not so definite in cases where only a segment of colon is involved. Buie, in this connection, states: "It is possible to be almost definite in the statement that usually only those instances in which the entire colon is involved by polypoid disease fit into the heredo-familial classification." Stewart[65] also agrees when discussing polyposis intestini (entire colon involved) that "this would appear to be merely an extreme grade of the condition of multiple polypi (segmental) already mentioned, were it not that there is a constitutional hereditary factor non-existent in the more banal variety."

The term heredofamilial tendency in this disease implies that the epithelial covering in the colon possesses some factor which predisposes it to tumor formation. In other words, there is present a mucosa which may have a "lowered threshold to stimuli," or else the inhibitive powers governing regulated growth are lost.[60] When these inherent factors exist, stimuli, which are normally present, are often sufficient to produce a proliferative response.

From an experimental point of view, very little has been done on the production of polyps in laboratory animals. Hoelzel and Da Costa[35] claimed to have produced polyps in the colons of rats by feeding them inert material, such as kaolin, barium, and talcum. This work, however, has not been repeated with similar results.[44]

INCIDENCE

Although multiple polypoid disease is usually considered a rarity, such might not be the case if routine examinations of the rectum and colon were done. Buie reports that at the Mayo Clinic between 1925-1935 there were 1,234 patients with polypoid disease. One of every 35 patients who complained of a disturbed function of the colon presented this condition.

Lawrence[42] found 166 cases of polypoid disease in 7,000 autopsies at Cook County Hospital (2.37 per cent).

Feyrter[29] examined 1,800 consecutive colons at autopsy and found polyps in 386 cases (21.4 per cent).

AGE

Multiple polypoid disease of the entire colon is said to be most common between the ages of 15 to 35 years. Hullsiek[39] found the average age to be 30.9 years in the 127 cases he reviewed from the literature. Doering,[22] in an analysis of 52 cases, also believes that this age group is the most commonly affected. In his analysis he found the youngest to be 5 years and the oldest 62. McKenney[47] reported a case in a child 2 years of age.

Polyps incidentally discovered in routine autopsies were found to be more numerous in older individuals. Lawrence[42] after studying 166 colons with multiple polypoid disease found 87.4 per cent to be over 40 years of age. Lawrence's figures differ from those of Hullsiek and Doering because he undoubtedly is speaking of multiple polypoid disease while they refer to multiple polypoid disease of the entire colon. The variance in these figures might infer that the two conditions are different clinical entities.

SEX

Most investigators agree that multiple polypoid disease of the entire colon is more common in males than females. In segmental multiple polypoid disease the incidence is about equally distributed.

NUMBER OF POLYPS AND SEGMENTAL DISTRIBUTION

The distal colon and rectum are involved most frequently. Soper found the rectum to be involved with polyps in 95 per cent of 61 cases. Thorbecke[69] also discovered this to be true in 80 per cent of his cases. He found that in 31 out of 54 cases in which rectal polyps were discovered there also existed polyps higher in the colon.

Lawrence[42] found that in all but 64 of 166 cases the distribution was restricted to a particular site. The distribution in his cases is shown in Table I:

TABLE I

POLYPS OF THE COLON (IN 166 CASES) IN 7,000 AUTOPSIES

	NO.	PER CENT
Cecum	46	16.1
Ascending	48	16.7
Hepatic	18	6.3
Transverse	48	16.7
Splenic	23	8.0
Descending	48	16.7
Sigmoid	56	19.5
	287	100.0

The number of polyps found in the 166 cases is as follows:

Single polyps	71
Double polyps	28
Triple polyps	27
Many polyps	37
Throughout colon	13

Stewart[65] found the following in 127 cases:

Single polyps	70
Several polyps	43
Large number	14

From the above it will be seen that multiple polypoid disease of the entire colon is relatively rare compared with the number of cases in which a single polyp is present or in which the distribution of polypoid disease is limited to a segment of the colon.

SYMPTOMS

The symptoms in this disease vary to a great extent with the location and extent of the pathology present. Quite frequently the entire colon has been involved with only a minimum of symptoms and with little discomfort to the patient. However, changes in bowel habit are usually the first noted. This may vary from an occasional soft stool to a profound diarrhea. Accompanying these changes, blood and mucus are often discovered in the stool. The loss of blood may be sufficient to produce a marked anemia. Indefinite abdominal pain[13] is often present, although the pain is usually located over the site of pathology.[67] At times, intermittent, crampy, colicky pain may be the first symptom. This is often indicative of a partial intussusception[9] caused by violent peristaltic contractions. Audible abdominal noises may be noticed. Tenesmus is most frequent when polyps are located in the distal colon and rectum.

DIAGNOSIS

A carefully taken history, together with an examination of the rectum and distal colon, is usually sufficient to suggest the diagnosis. The stool should be submitted to a thorough examination to determine the presence of amoebae or other parasites. Suffice it to say that all patients should be given the benefits of a careful proctoscopic examination. When properly done, the lower 20 cm. of the bowel can be examined without discomfort to the patient. When polyps are found, the entire colon should be submitted to a roentgenologic examination to ascertain the presence of polyps higher in the colon. To accomplish this the double contrast method is employed. The painting of the bowel wall after it has been distended with air and the visualization by stereoroentgenographs, as advocated by Weber,[71] serve as the best available means of investigating the colon. An expert roentgenologist, by using this method, can visualize polyps less than 1 cm. in diameter.

TREATMENT

Until the etiology of polypoid disease is better understood, all therapeutic measures must be directed at the eradication of the tumor tissue. Dietary measures aimed at the reduction of roughage in the diet have

been unsuccessful. Astringent drugs, such as quinine, tannic acid, and magnesium chloride, have been used in the form of colonic irrigations without results.

Deep x-ray therapy has been employed by Barker,[3] McKenney,[47] and others.[1, 11] Its use has been attended by the passage of grapelike, necrotic growths found in the stool with an improvement of symptoms. However, no case has been reported in which all of the polyps have disappeared following this therapy.

Fulguration of all polyps within the reach of the sigmoidoscope should be carried out without delay. To one experienced in the use of the sigmoidoscope, polyps may be fulgurated above the rectosigmoid. The danger of fulgurating too extensively, with resulting perforation, should always be kept in mind.

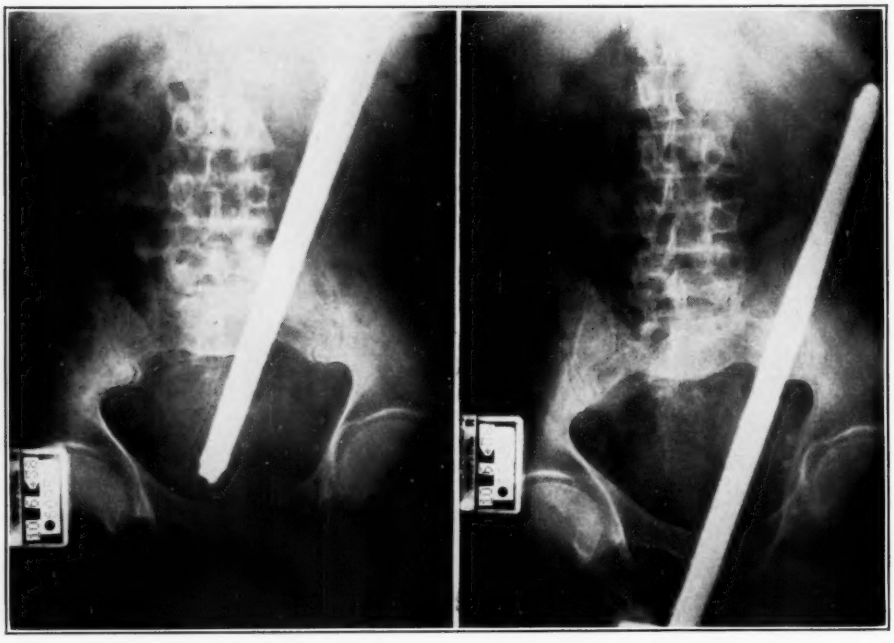
Various surgical procedures have been advocated.[7, 12, 21] Divergence of the fecal current by the use of ileostomy and colostomy occasionally has been followed by the disappearance of the tumors in the portion of the bowel put to rest.[33] Isolated polyps may be excised[58] or the segment of the bowel embracing these tumors may be resected.[10, 19, 20, 51]

When multiple polypoid disease of the entire colon is present, total colectomy[40, 55, 56] offers the only hope for those unfortunate individuals affected. An ileostomy is done when the entire colon and rectum are resected. If the rectum and lower sigmoid are preserved, an ileosigmoidostomy[18] is done prior to resection of the remaining colon. In this procedure all existing polyps of the rectum and remaining sigmoid are removed by fulguration from below.

Mayo and Wakefield[46] have reported a procedure used in dealing with multiple polypoid disease of the entire colon in which an ileosigmoidostomy and colectomy were done. The distal sigmoid was brought out as a colostomy. Through this opening all polyps which could not be reached from below were fulgurated. Later the colostomy was closed. Fansler,[28] in discussing this operation, cited a case in which he had fulgurated polyps through a colostomy. He also mentions the potentialities of such a procedure.

As it was stated above, all therapeutic measures should be aimed at the early eradication of the tumor tissue. In many cases the polyps may be few in number and limited to a segment of the colon.[45] Also, cases may be encountered in which a few polyps are distributed in more than one segment of the large bowel. These conditions are often seen in young individuals who are otherwise healthy. To recommend a radical procedure, such as a colectomy, imposes on the surgeon a great responsibility and on the patient a great danger. In many of the cases most of the colon is normal from a clinical standpoint. And who, in our present state of knowledge of this disease, is in a position to say that the entire

colon should be sacrificed? In this connection one is confronted with many perplexing questions. How long have the polyps been present? Is a colon, in which only a segment is involved, destined in time to become studded with polyps? Or will malignancy and death occur before sufficient time has elapsed for the disease to involve the entire colon? Is segmental polypoid disease a different pathologic entity from multiple polypoid disease of the entire colon? Is the heredofamilial factor present to the same degree in both types? Does malignant degeneration occur equally in both types? If this is so, why are polyps discovered so frequently at autopsy in the aged? Are polyps found late in life all on an inflammatory basis or have they been present since birth? Could all



A. *B.*

Fig. 1.—*A*, Sigmoidoscope entering a left colostomy and passing into sigmoid colon; *B*, sigmoidoscope entering a left colostomy and passing into the splenic flexure.

polyps of the colon be caused by an organism which so far has not been isolated? These questions in our present state of knowledge cannot be accurately answered.

PROPOSED SURGICAL PROCEDURE

When a segment of the colon is involved with polypoid disease or when only a relatively few polyps are present throughout the colon, it would seem rational that an attempt should be made to remove successfully the tumors without sacrificing the entire colon. Fulguration of the tumors through a properly placed colostomy appears to be the only possible method by which this objective could be attained. With this thought in mind, several patients with colostomies were studied at Cook County

Hospital. Buie sigmoidoscopes of various lengths were introduced through the colostomy openings to determine the possibility of visualizing the interior of the large bowel. It was found, by careful manipulation of the scopes, that the interior of almost the entire colon could be visualized. This was accomplished despite the fact that the colostomy openings were often small due to the contraction of the surrounding structures. Had the colostomy been made with the idea in mind of passing a sigmoidoscope, the visualization of the interior of the bowel would have been greatly facilitated. X-ray pictures have been taken with the sigmoidoscope inserted through a colostomy in the left colon (Fig. 1).

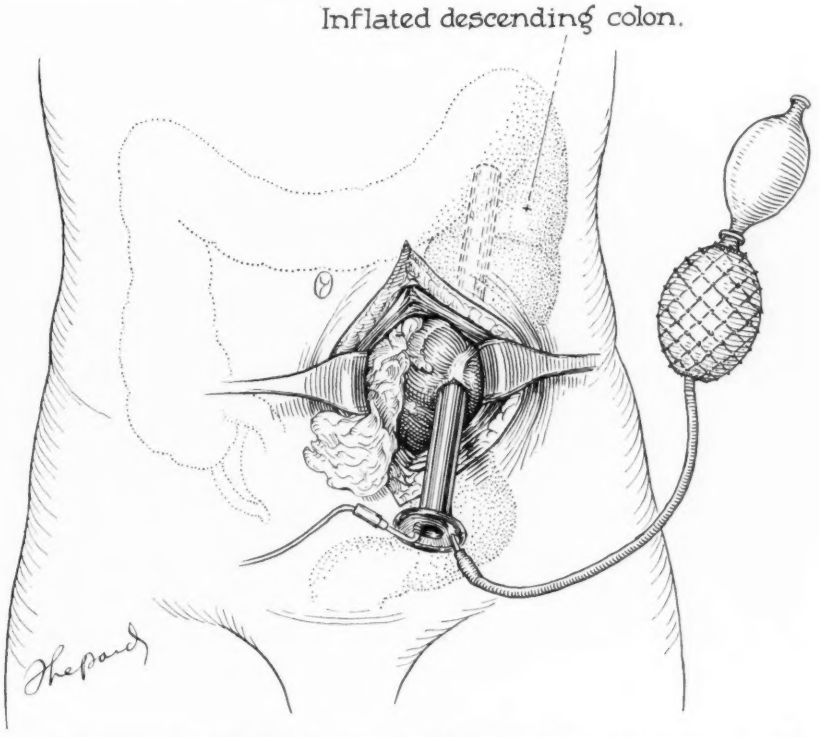


Fig. 2.—Diagrammatic drawing showing the introduction of the scope at the time of one-stage operation.

The success with which the interior of the bowel could be seen strongly suggests that polyps in the colon could easily be fulgurated by this method.

The procedure could be carried out in one stage or two stages (Figs. 2-4). It is proposed that if polyps are present in the left colon they could be fulgurated through a colostomy in the left colon (Fig. 4). A colostomy in continuity[17, 32] would obviate the necessity of crushing a spur when fulguration of the tumors was completed. The colostomy could be closed over and the colon replaced into the peritoneal cavity.[16] Protective walling off of the peritoneal cavity[53, 57] would safeguard against peritonitis from the exteriorized bowel.

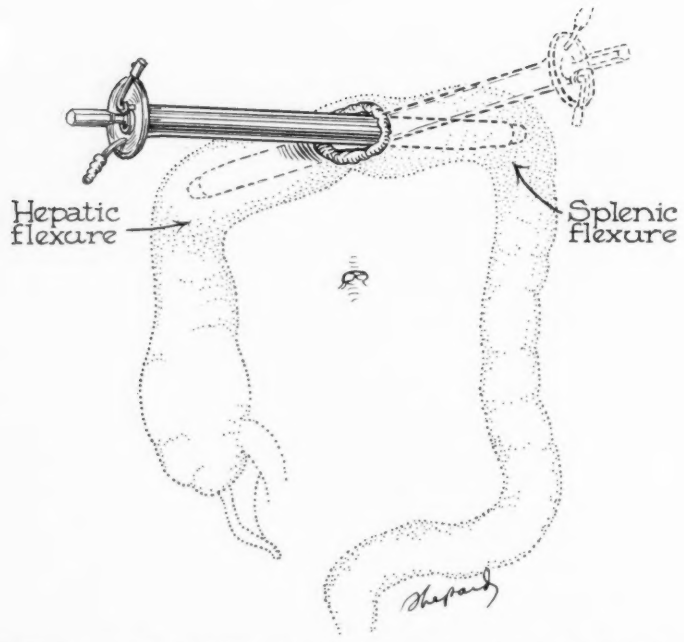


Fig. 3.—Diagrammatic drawing showing scopes entering a transverse colostomy. Polyps located in the transverse colon, hepatic or splenic flexures could be fulgurated by this proposed two-stage procedure.

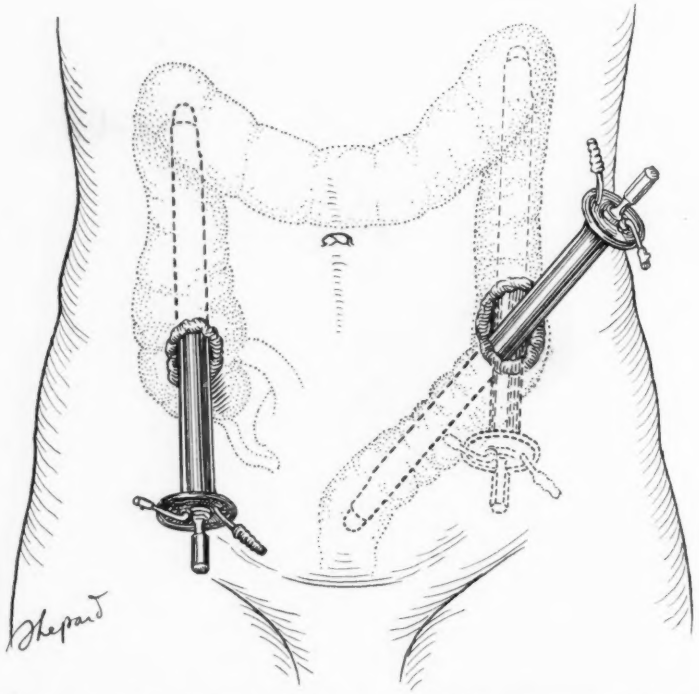


Fig. 4.—Diagrammatic drawing showing location of colostomies through which polyps in the right and left colon could be fulgurated; two-stage procedure.

In a like manner, polyps located in the hepatic and splenic flexures, as well as the transverse colon, could be fulgurated through a transverse colostomy (Fig. 3). A cecostomy[48] would serve as the best site for the introduction of the sigmoidoscope to fulgurate polyps located in the cecum and ascending colon (Fig. 4).

Exteriorizing the colon, thereby making a two-stage procedure, permits painstaking fulguration and observation of the healing areas. Should it be found that a portion of the tumor had been inadvertently missed, subsequent fulguration is possible by this two-stage procedure.

Fulguration of polyps could also be done in a one-stage operation (Fig. 2). By carefully walling off the field to prevent contamination, an opening could be made along the anterior longitudinal band, large enough to admit the sigmoidoscope. The assistant surgeon could be helpful in manipulating the scope from the peritoneal side of the bowel. In this way fulguration would be facilitated and the sites could be inspected for possible perforation. Following the thorough fulguration of all polyps in the segment, the opening in the wall of the colon could be closed in the usual manner.

The advantages of the one-stage procedure are that the patient has but one operation and does not have to tolerate a colostomy (Fig. 2). The fulguration in this operation must be complete because there is not another opportunity for inspection and subsequent fulguration. The chances of peritoneal soiling are greatly increased in the one-stage procedure.

The danger of perforation of the bowel wall, as a result of fulguration, is always present. However, it is certainly no greater than when polyps located in the sigmoid, above the peritoneal reflexion, are fulgurated through a scope passed from below.

When one is confronted with a patient with multiple polypoid disease of the entire colon, in whom a radical procedure, such as a colectomy, is contraindicated, the method proposed may be of some value. By painstaking fulguration through multiple colostomies, large numbers of polyps could be removed, thus decreasing the malignant potentialities of the disease.

SUMMARY AND CONCLUSIONS

1. The terminology and classifications used in the literature regarding polypoid lesions in the colon are confusing.

2. There is definite evidence that polypoid lesions of the colon undergo malignant changes.

3. The etiology of this disease is not understood. It appears that multiple polypoid disease limited to a segment of colon differs etiologically and pathologically from multiple polypoid disease of the entire colon.

4. Sigmoidoscopic examinations and double contrast stereoroentgenographs establish the diagnosis of this disease.

5. The various types of treatment are outlined.

6. It is proposed that polypoid lesions in the colon could be fulgurated through properly placed colostomies.

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GRADUAL COMPLETE OCCLUSION OF THE CELIAC AXIS, THE SUPERIOR AND INFERIOR MESENTERIC ARTERIES, WITH SURVIVAL OF ANIMALS: EFFECTS OF ISCHEMIA ON BLOOD PRESSURE

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RENEWED interest in ischemia as a factor in the causation of hypertension has been stimulated by the work of Goldblatt and his associates.[1] They found that a persistent elevation of the systolic blood pressure may be associated with the renal ischemia that is produced by partially occluding the renal arteries.

Longcope and McClintock[2] in 1910 determined the effects on the blood pressure of dogs of constriction of the celiac axis and superior mesenteric artery by means of aluminum bands. They found that neither cardiac hypertrophy nor hypertension followed the narrowing of the mouths of these vessels. Autopsies several months following the operations showed no abnormalities except perhaps some congestion of the liver. In none of the animals were both the celiac axis and superior mesenteric artery completely occluded. Jansen, Tams, and Achelis,[3] in acute experiments, found that the rise in pressure resulting from constricting the splanchnic vessels was increased by additional obstruction of the vessels of an extremity.

The abdominal organs, excepting the kidneys and adrenals, are supplied arterial blood in the main by the celiac axis and the superior and inferior mesenteric arteries. If all of these vessels are occluded at one time, death results. The purpose of the present studies was to determine whether or not dogs will tolerate complete occlusion of these vessels in stages and, if so, what the effect on the arterial blood pressure would be. In additional experiments the effects on the blood pressure of occlusion of the main arteries of the extremities and of the head were studied.

METHODS

Dogs were used in all studies. The blood pressure in all instances was determined by puncturing the femoral artery with a needle which was connected to a mercury manometer. The value obtained is approximately the mean blood pressure. All of the operations were performed under ether anesthesia. The celiac axis and the superior mesenteric

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artery were approached through an incision in the left flank and the inferior mesenteric artery was exposed through a low abdominal incision. Although there was some variation, the usual order of operations was as follows: At the first operation, the celiac axis and superior mesenteric artery were exposed near the aorta and were constricted by Goldblatt clamps.* After several weeks, the interval depending upon the condition of the animal, this constriction was increased. Several weeks subsequently, the inferior mesenteric artery was doubly ligated and divided. Approximately one month subsequently, constriction of the celiac axis and the superior mesenteric artery was made complete. The arterial blood pressure was determined frequently.

RESULTS

A total of twenty-nine animals was used in this study. Fourteen of these died at varying times following the first operation. A large proportion of these deaths occurred in the earlier experiments and were due almost certainly to too great constriction of the celiac axis and superior mesenteric artery. A number of these passed stools containing blood. Five of the animals died following the second operation, two after the third, and one following the fourth. The last operation on the latter animal had been performed sixteen days previously. The body weight of most of them declined markedly. The remaining seven animals survived complete occlusion of the three main vessels and apparently remained in good health. There was some loss in weight during the process of occluding the vessels, but this was regained subsequently.

Since the alterations in blood pressure were not great, they will not be recorded in detail. None of the animals exhibited a marked increase in the pressure. Unless the animal became quite ill following the operation, there was usually a rise in blood pressure of approximately 20 mm. Hg. which tended to return to the control level after a few days. Subsequent additional constriction was usually associated with a slight elevation in pressure. Two animals showed a persistent elevation of approximately 15 mm. during the two months periods that the pressure was followed after having caused complete constriction of the three main vessels. Palpation of the arteries of the mesentery of the intestine failed to reveal pulsation in two of the three instances in which this region was explored after the three main vessels had been occluded. Despite the absence of a palpable pulsation, the animals ate heartily and appeared to be well.

Autopsies were performed on three of the animals in which the three vessels had been completely constricted. The vessels were found to be entirely occluded by an organized clot. The Goldblatt clamps had cut through and were lying in a pocket of fibrous tissue. The occlusion had been complete for at least six months in one of these animals. No gross

*Furnished through the courtesy of Dr. Harry Goldblatt, Cleveland, Ohio.

abnormalities of the abdominal viscera were observed. The lumbar arteries were believed to be somewhat enlarged. No attempt was made to determine the collateral pathways by which the blood reached the organs normally supplied in the main by the three large vessels.

Five animals with complete occlusion of the three vessels are alive at present and are being used in other studies in which additional vessels are constricted. The period of complete occlusion of the celiac axis, the superior and inferior mesenteric arteries in these animals varies from three to nine months. They appear to be entirely normal.

In addition to the studies which have been enumerated, the effects of occlusion of other large arteries on the systemic blood pressure have been determined. The first of these consisted of gradual occlusion of the main arteries to the liver by a procedure similar to that described recently by Huggins and Post.[4] When the occlusion was produced gradually, the animals remained in good condition. No elevation in the arterial blood pressure was observed in the two animals which were studied. The second group consisted of seven experiments in which the two common iliacs and the two subclavian arteries were doubly ligated and divided. The blood pressure in these studies was determined in the carotid artery which was placed beneath the skin of the neck. Several of the animals showed a temporary rise in pressure of about 10 mm., but this was not sustained. The third group consisted of five experiments in which the two common carotid arteries and the two vertebrals were doubly ligated and divided. This was usually done in two stages, one carotid and both vertebrals being occluded at the first operation. Four of the five animals showed for a few days a temporary rise in pressure ranging from 10 to 60 mm. Both vertebrals and both carotids were ligated at one time in the experiment in which the greatest rise in pressure was encountered. The pressure remained definitely elevated for more than two weeks in this animal.

DISCUSSION

The main objects of the present study were to determine: first, whether or not dogs will survive gradual permanent occlusion of the main vessels to the intestinal tract and associated organs; and second, the effect of these procedures on the blood pressure. It was rather a surprise to us that a good many of the animals remained in remarkably good condition after the three main vessels had been occluded. It is likely that the percentage of survivals would have been greater if the degree of constriction had been smaller at the onset and if the time interval between operations had been lengthened. As has been stated, a large proportion of the dogs lost a great deal of weight. It seems likely that this was due either to the repeated operative procedures or to the effect of intestinal ischemia on the digestive functions. These points should be investigated further. The observation that animals may re-

main in good condition without pulsations in the arteries to the intestinal tract should be confirmed.

As stated, Goldblatt and his associates[1] found that hypertension may be produced by causing renal ischemia. They found that partial occlusion of the splenic and femoral arteries did not result in hypertension. We have found that a permanent elevation in the systemic blood pressure is not associated with occlusion of the main arteries of the extremities, of the head, of the liver, or of the intestinal tract, including the spleen, pancreas and liver. The results indicate that ischemia of the kidneys is necessary for the production of this type of hypertension. Although no definite conclusions can be drawn, the results substantiate the rather generally accepted view that arteriosclerosis of the large arteries, excepting the renals, is not a frequent cause of hypertension. Apparently the narrowing of the vessels is soon compensated for by collateral anastomoses. Longcope and McClintock[2] studied on autopsy specimens the relationship between sclerosis of the branches of the abdominal aorta and the weight of the heart. They state: "Indeed, of the twenty-one cases in which the splanchnic vessels were narrowed, only seven were associated with any degree of cardiac hypertrophy and in all seven cases a definite chronic nephritis coexisted."

The effect of renal ischemia in animals in which large vessels elsewhere have been occluded previously is being investigated.

SUMMARY

Gradual complete occlusion of the celiac axis and the superior and inferior mesenteric arteries may be produced in dogs without causing death or a permanent impairment in health. A sustained elevation in the systemic blood pressure was not encountered in these experiments. Neither is a permanent elevation in pressure associated with occlusion of the main arteries to the extremities or head.

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EFFECT OF PARTIAL GASTRECTOMY ON ACIDITY AND PEPTIC ACTIVITY OF GASTRIC JUICE

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AN OPPORTUNITY of studying certain problems in the control of gastric secretion has been afforded by follow-up observations on patients with partial gastrectomy. The fact that this operation recently has been more widely advocated in the surgical treatment of selected cases of peptic ulcer suggests the importance of understanding the physiologic principles underlying the successful application of this procedure.

It is generally believed that the antral portion of the stomach controls the chemical or so-called second phase of gastric secretion and that removal of the antrum results in a decrease in the amount of acid and pepsin secreted.[1] Studies in the dog have shown that free hydrochloric acid is usually not present in the gastric contents after partial gastrectomy. By means of a Pavlov pouch, however, it may be demonstrated that the stomach still retains some capacity to secrete hydrochloric acid even after complete removal of the antrum. It is believed that this secretion is usually neutralized in the main stomach by regurgitated intestinal juices and anacidity results.

There is a considerable difference of opinion concerning the effect of partial gastrectomy on gastric acidity in man. The proportion of cases in which achlorhydria has been demonstrated varies widely and there is disagreement regarding the interpretations of the findings. If, however, the reported results are classified according to the technique of gastric analysis employed, these variations appear to be clarified (Table I).

When a single aspiration of stomach contents is carried out approximately one hour after a test meal, no free acid is found in the majority of cases.[2-4] If aspirations are performed at repeated intervals after a test meal, free acid is more frequently demonstrable,[5] and if a technique of continuous suction be employed[6] free hydrochloric acid can be shown to be present in most instances. Free hydrochloric acid also may be found in a higher proportion of cases if histamine is used as a stimulus to secretion.[7-9]

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TABLE I

INCIDENCE OF ACHLORHYDRIA AFTER PARTIAL GASTRECTOMY FOUND WITH DIFFERENT METHODS OF GASTRIC ANALYSIS*

INVESTIGATOR	METHOD OF GASTRIC ANALYSIS	NUMBER OF CASES EXAMINED	PERCENTAGE OF CASES WITH ACHLORHYDRIA
Lorenz and Schur, 1922	Simple test meal	55	75%
Smidt, 1924	Simple test meal	100	79%
Lewisohn, 1923	Simple test meal	10	60%
Strauss et al., 1937	Histamine or test meal	31	58%
Gorvett and Talbot, 1937	Fractional test and histamine	26	65%
Neumann, 1932	Fractional alcohol meal	44	57%
Klein, 1935	Fractional gruel meal	35	32%†
Comfort and Osterberg, 1931	Histamine and continuous aspiration	?	20%
Necheles and Scheman, 1934	Continuous suction	20	10%

*Most of the groups enumerated in this table include several types of gastric resection.

†Klein found a higher incidence of achlorhydria six month after operation.

Although differences of technique appear to offer at least a partial explanation of the discrepant results obtained by different investigators, other factors may play a role. In any series of patients subjected to partial gastrectomy, the size of the resected portion of the stomach varies considerably. It has been stated that those patients in whom the antral portion of the stomach has not been completely removed continue to show free hydrochloric acid.[2, 3] Others have maintained that anacidity develops slowly after operation and that the incidence of achlorhydria depends upon the postoperative time interval.[5] The site of the original ulcer has also been thought to be influential in determining the effects of this operation upon gastric secretion, anacidity being found more frequently by some workers after resection for gastric ulcer.

A few studies of gastric pepsin after partial gastrectomy have been carried out. Lorenz and Schur,[2] using the Mett tube method reported that the peptic activity of gastric juice is sometimes diminished after operation but frequently remains within normal limits. More recently, Neumann[10] has reported that pepsin is either absent or is present in only traces in those patients with anacidity after operation. The modern and more precise techniques for peptic determination have not been used.

In the present study we have analyzed the gastric secretion of a series of patients after partial gastrectomy for peptic ulcer in an attempt to clarify some of the above problems. It was also hoped that this study might yield an explanation for the success or failure of the operation in the treatment of ulcer.

Twenty-six patients upon whom partial gastric resection had been performed for peptic ulcer were selected at random from the Surgical Follow-up Clinic of the Presbyterian Hospital. Eleven patients had

originally suffered from gastric ulcer; 13, from duodenal ulcer; and 2, from combined ulcers. An anterior or posterior Polya operation had been performed in 19 cases and the Billroth II operation in 7 cases. Anteoperative gastric analyses, secured in 13 cases, had shown the presence of free hydrochloric acid. The interval which had elapsed between the operation and the time of examination varied from one month to nineteen years.

The gastric contents were obtained by single aspiration one hour after an Ewald test meal. After filtration of the gastric juice, the free and combined acidities were determined by titration with sodium hydroxide. Pepsin determinations were carried out by the hemoglobin digestion method of Anson and Mirsky.[11, 12] For the sake of simplicity, results are expressed in milligrams of pepsin U.S.P. 1:4,000. Hydrogen ion concentration determinations were done colorimetrically. No attempt was made to obtain or to estimate the total volume of gastric contents but in most instances the quantity of gastric juice obtained by aspiration was small.

Gastric Acidity (Table II).—Free hydrochloric acid was absent in 22 cases, diminished in 3 cases, and within normal limits in 1 case. Combined acidity exceeded 10 degrees in 16 of the 26 cases and was as high as 24 degrees in 1 patient with achlorhydria. The pH of the gastric contents not containing free hydrochloric acid varied between 4.2 and 6.4 and was in the neighborhood of 5.0 in the majority of instances. The pH of the specimens containing free acid was approximately 1.2 to 1.4.

In analyzing these results, no explanation could be found for the failure of four of our patients to develop anacidity. There was no relation between the postoperative time interval and the presence of free acid or the amount of combined acid. Achlorhydria was usually manifested both in recently operated cases and in patients operated upon from five to fifteen years previously. There was no tendency for free acidity to persist in patients who had originally suffered from ulcer of the duodenum, as was suggested by Klein.[4]

Two of the four patients (Cases 20 and 26) whose gastric secretion still contained free hydrochloric acid had had very extensive gastric resections. It was impossible to determine in retrospect the amount of stomach which had been removed at operation in many instances. The impression was gained, however, that the antral portion of the stomach had not been completely removed in some of our patients with anacidity.

Intestinal Regurgitation (Table II).—The presence of regurgitated intestinal juice in the gastric contents was indicated by a yellow or green color in all but two of our patients. One of the remaining two colorless specimens contained free hydrochloric acid.

Peptic Activity (Table II).—Determinations of pepsin were carried out in 24 cases. The results show a marked diminution in the peptic

TABLE II

GASTRIC ACIDITY AND PEPSIN IN 26 CASES AFTER PARTIAL GASTRECTOMY

CASE	SEX	PRESENT AGE	LOCATION OF ORIGINAL ULCER	TYPE OF OPERATION	POSTOPERATIVE TIME INTERVAL	SYMPTOMS SINCE OPERATION	COLOR	EWALD TEST MEAL		
								FREE HCL	TOTAL ACID	PEPSIN MG. PER C.C.
1	F	57	Gastric	Polya (midgastric)	19 yr.	None	Yellow	12	37	1.2
2	M	39	Gastric	Billroth II (pylorectomy)	15 yr.	None	Yellow	0	10	0.7
3	M	69	Gastric and duodenal	Billroth II; Enteroenterostomy	15 yr.	None	Yellow	0	14	1.4
4	F	46	Duodenal	Billroth II (pylorectomy)	14 yr.	Three periods of acute melena ? jejunal ulcer	Yellow	0	10	1.1
5	M	45	Gastric	Polya; enteroenterostomy	12 yr.	None	Clear	0	4	0.2
6	F	58	Gastric	Billroth II (pylorectomy)	12 yr.	None	Yellow	0	8	--
7	F	47	Gastric and duodenal	Billroth II (pylorectomy)	12 yr.	None	Yellow	0	8	0.9
8	F	57	Gastric	Anterior Polya Enteroenterostomy	7 yr.	None	Yellow	0	10	--
9	F	27	Duodenal	Posterior Polya (pylorus) enteroenterostomy	7 yr.	None	Yellow	24	44	1.8
10	M	64	Gastric	Billroth II	6 yr.	None	Yellow	0	14	0.6
11	M	47	Duodenal	Billroth II Enteroenterostomy	5 yr.	None	Yellow	0	16	0.0
12	M	42	Gastric	Posterior Polya Enteroenterostomy	5 yr.	None	Yellow	0	16	0.2
13	F	64	Gastric	Posterior Polya	3 yr.	None	Yellow	0	12	2.0
14	M	31	Duodenal	Anterior Polya	2 yr.	None	Yellow	0	16	0.8
15	M	33	Duodenal	Posterior Polya	2 yr.	None	Yellow	0	16	0.6
16	M	54	Duodenal	Posterior Polya	2 yr.	None	Yellow	0	8	0.0
17	F	58	Duodenal	Posterior Polya	2 yr.	None	Yellow	0	16	4.0
18	M	41	Duodenal	Posterior Polya	1 yr.	Recurrent pain; marginal ulcer		0	3	0.5
19	F	57	Gastric	Anterior Polya	1 yr.	None	Yellow	0	24	0.1
20	M	59	Duodenal	Polya	1 yr.	Jejunal ulcer excised at subsequent operation		42	60	2.8
21	M	41	Duodenal	Posterior Polya	1 yr.	1 hemorrhage	Yellow	0	8	0.2
22	M	47	Duodenal	Anterior Polya	1 yr.	None	Yellow	0	12	0.1
23	M	33	Duodenal	Anterior Polya	6 mon.	None	Yellow	0	18	0.6
24	M	40	Gastric	Anterior Polya	4 mon.	None	Yellow	0	18	0.4
25	M	40	Gastric	Anterior Polya	1 mon.	None	Yellow	0	10	0.3
26	F	52	Duodenal	Posterior Polya	1 mon.	None	Clear	20	36	5.4

activity of gastric juice after partial gastrectomy in almost all instances. In all but 3 of our cases, the amount of pepsin was found to be below the range found in unoperated patients with peptic ulcer.* In two instances no peptic activity was demonstrable. The specimens which contained free hydrochloric acid showed relatively large amounts of peptic activity, in accord with the usual finding of a proportionality between gastric acidity and peptic activity. No relation was apparent between the amount of pepsin secretion in individual cases and the postoperative time interval.

Follow-Up Results.—All of the patients included in this series have been carefully followed by the Surgical Clinic. Twenty-two members of the group, 12 of whom have been followed for over three years, have remained completely free from symptoms of ulcer during their entire follow-up period. The remaining four patients have suffered from recurrent abdominal pain or melena, attributed in each instance to jejunal ulcer. In one of these patients (Case 20) the presence of jejunal ulcer was proved at exploration. The gastric juice of this patient contained free hydrochloric acid. The other three patients (Cases 4, 18, and 21) who had had recurrent symptoms, however, showed anacidity. Our studies of gastric secretion offer no explanation for the therapeutic failure in these cases. In most instances, however, the occurrence of achlorhydria after partial gastrectomy for peptic ulcer offers a satisfactory explanation for the high percentage of successful results following that operation.

DISCUSSION

In the light of these findings several explanations for the reduced acidity resulting from partial gastrectomy may be considered. Gastric acidity depends upon the volume of acid secretion, the rate of emptying of the stomach and the presence of neutralizing or buffering substances. The finding of moderate amounts of combined acid and peptic activity in the majority of our cases indicates that the stomach usually continues to secrete in response to food after partial gastrectomy. It is impossible to determine directly the volume of such secretion. One can only surmise on the basis of animal experimentation[1] that a reduction in volume has occurred. Accelerated emptying of the test meal by the stomach after partial gastrectomy might be expected to decrease the period of gastric stimulation if the chemical phase of secretion is still partly effective. Our failure to obtain large volumes of gastric juice in most cases would suggest that the peak of secretion after the Ewald meal is passed in less than one hour. Admixture of alkaline juices from the small intestine is undoubtedly an important factor in reducing acidity after

*The rough parallelism between acid and pepsin secretion is exemplified in uncomplicated ulcer where the pepsin secretion tends to be high. The range of pepsin occurring in a series of patients with simple duodenal ulcer reported by Mullins and Flood[12] was 2.1 to 11.7 mg. per c.c. (U.S.P. pepsin 1:4,000). In gastric ulcer the results fall within the same range.[13]

partial gastrectomy and was manifested by the presence of intestinal juices in the gastric contents of nearly all of our cases.

The lowered peptic activity of gastric juice after partial gastrectomy may be attributed either to partial destruction of the enzyme or to diminished secretion. It is well known that the addition of alkali to an acid solution of pepsin irreversibly destroys pepsin. Thus, inactivation of pepsin by alkaline juices regurgitated from the intestine probably takes place after partial gastrectomy.

The evidence available supports the view that the anacidity after partial gastrectomy is due both to a reduction in secretion and to regurgitation of alkaline intestinal juices. The relative quantitative importance of these two factors has yet to be determined. The marked lowering of the level of gastric acidity after partial resection affords a reasonable explanation for the high measure of success which this operation offers in the prevention of recurrences of peptic ulcer. The fact that ulcer may sometimes recur after operation in spite of this lowered acidity suggests that other unknown factors in addition to acid-pepsin digestion may play a role in the genesis of peptic ulcer.

SUMMARY

1. Gastric secretion after patrial gastrectomy for peptic ulcer was studied in a series of 26 patients. Operation had been performed one month to nineteen years previously.

2. Twenty-two patients (85 per cent) exhibited achlorhydria after a test meal.

3. Gastric pepsin was markedly diminished in 21 of 24 cases studied (88 per cent).

4. Follow-up observations indicated in general that those patients with anacidity remained asymptomatic. However, three patients with anacidity had recurrent symptoms of ulcer.

5. The reduction in the level of gastric acidity occurring after partial gastrectomy explains the success of that operation in the prevention of recurrence of ulcer.

6. The reduced acidity is probably due both to the abolition of the chemical phase of gastric secretion and to regurgitation of alkaline intestinal juices.

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TUBERCULOSIS OF THE STOMACH

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IT IS a curious fact that tuberculosis seldom attacks the stomach. For example, in the study of 1,400 autopsies upon tuberculous subjects, Crawford and Sawyer[5] did not find a single instance of gastric involvement; whereas, the incidence of tuberculous lesions of the ileum and colon reached 70 per cent. The remarkable resistance of the stomach to this infection becomes most impressive if we recall the routine clinical use made of the sputum to detect the presence of tubercle bacilli and recall also the fundamental character of the act of swallowing saliva, a necessity good manners imposes incessantly upon all of us, tuberculous or not. Clearly, potent bacteria reach the stomach often enough and in sufficient number to make a formidable attack upon that organ whenever individuals suffer from the commonplace respiratory types of tuberculosis. Why it does not happen so remains a moot question. Some distinguished pathologists have taught that the acidity of the gastric juice was the responsible protective factor; others have emphasized the rapid transportation of infectious material through the organ, an efficient degree of gastric motility. Of late it is the inclination of those giving the problem special study to point a close relationship between a low incidence of gastric tuberculosis and the meagre supply of lymphoid tissue in the wall of the stomach. In any case, a preliminary break in the continuity of the gastric mucosa seems essential to its penetration by the tubercle bacillus.

Rigid criteria for authentication of the pathologic diagnosis have served appreciably to limit the number of cases of gastric tuberculosis worthy of publication. From a review of the literature as far as 1917, Broders[1] gathered 307 presumptive cases, although the typical microscopic anatomy and acid-fast bacilli had been demonstrated only 50 times. In addition, the histologic evidence was adequate in 118 instances, but there no mention was made of the presence of organisms. Among the remaining cases, 59 were regarded as doubtful, while 89 were rejected altogether. Good[3] carried the compilation forward to the year 1931, collecting 194 cases which deserved consideration; in 52 the diagnosis was positive, in the others quite probable. Subsequently 17 completely established cases have been added to the list through the reports of Pop,[2] Price,[4] Genkin,[6] Knolflach,[7] Szacsvay,[8] Grayzel,[9] Walters and others,[10] Eusterman and Balfour.[11] The analysis of all the material available thus far yields 54 cases definitely proved and 157 probable, a total of 211 cases in medical literature to the end of 1937.

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The clinical manifestations of gastric tuberculosis vary with the way the tissues react to the invading organisms. Whenever the degree of cellular proliferation gives rise to a tuberculoma, both the symptoms and the roentgenologic findings resemble those associated with carcinoma. On the other hand, ulcerative lesions are productive of symptoms akin to those of peptic ulcer. Then again, but very rarely, miliary tuberculosis or tuberculous lymphangitis of the stomach may be encountered; in these circumstances no symptoms appear, at least none have been recognized. Pathognomonic roentgenologic details of gastric tuberculosis have yet to be described.

The demonstration of tuberculosis elsewhere in the body has not proved very helpful in the difficult task of differentiating gastric tuberculosis from carcinoma or from peptic ulcer. It is true, however, that roundly 50 per cent of the authenticated cases of gastric tuberculosis have occurred simultaneously with tuberculous foci in other organs, especially with the pulmonary variety.

Since there is slight, if any, disposition on the part of gastric tuberculosis to heal spontaneously and since with time its symptoms become more and more aggravating, occasionally surgical intervention has been required, as in the case herewith reported. The strength of the patient and the extent of the gastric lesion guide the surgeon in the type of operation he selects. Obviously, the more radical the resection, the greater the likelihood of eliminating the disease from the stomach. And, in a practical sense, nothing has been gained from the refinements of preoperative differential diagnosis, for the same technical principles prevail in the treatment here, as in peptic ulcer and carcinoma. A mortality of 21 per cent, according to Good, was associated with the operative treatment of 24 cases of gastric tuberculosis.

CASE REPORT

J. A. K. (No. 489-556), a Caucasian piano-maker, entered the Los Angeles County General Hospital, March 28, 1936. A mild, dry, nonproductive cough had persisted five years. There were no gastric symptoms until three years before admission, when he began to suffer from epigastric pain one to three hours after meals. This distress was relieved by drinking milk or beer.

Physical examination revealed signs of infiltration at the apices of both lungs, with cavitation on the left. Palpation of the abdomen disclosed a slightly tender mass 5 cm. in diameter in the left hypochondrium. By the benzidine test the stools were positive for occult blood. The sputum contained numerous acid-fast bacilli. Both the Wassermann and Kahn reactions were negative. Blood count: Hb. 75 per cent; R.B.C., 4,850,000; leucocytes, 9,400. Fractional gastric analysis with histamine gave a maximum total acidity of 50° and a free acidity of 32°. Urinalysis was negative.

Roentgenologic examination revealed no obstruction of the stomach, but there was a tender filling defect in the prepyloric region of the greater curvature, strongly suggestive of malignancy. There was chronic bilateral ulcerative tuberculosis of the lungs, far advanced.

The preoperative diagnosis included pulmonary tuberculosis and carcinoma of the prepyloric region of the stomach. On April 4, 1936, under cyclopropane, nitrous oxide, and avertin anesthesia, the abdomen was explored through a left paramedian incision. The viscera, other than the stomach, showed no abnormality. A grayish, infiltrating mass, approximately 5 inches long, was visible in the prepyloric region, and along the greater curvature numerous mesenteric lymph glands were enlarged. Grossly, the appearance of the lesion was suggestive of carcinoma, but upon palpation the mass was found less firm and not so thick as in the average case of carcinoma.

Fig. 1.—Tuberculosis of stomach; preoperative gastric x-ray.

A partial gastric resection was performed, removing a segment extending from 1 inch distal to 7 inches proximal to the pylorus. After closure of the duodenal stump, an antiperistaltic, retrocolic Polya anastomosis was made between the distal end of the stomach and the first portion of the jejunum. The abdomen was closed without drainage. The postoperative course was uncomplicated, save for slow healing of the wound, which finally closed completely. On July 4, 1936, no evidence of obstruction was found during roentgenologic examination of the stomach. On the other hand, the chest study showed an increase in the nodular infiltration of the

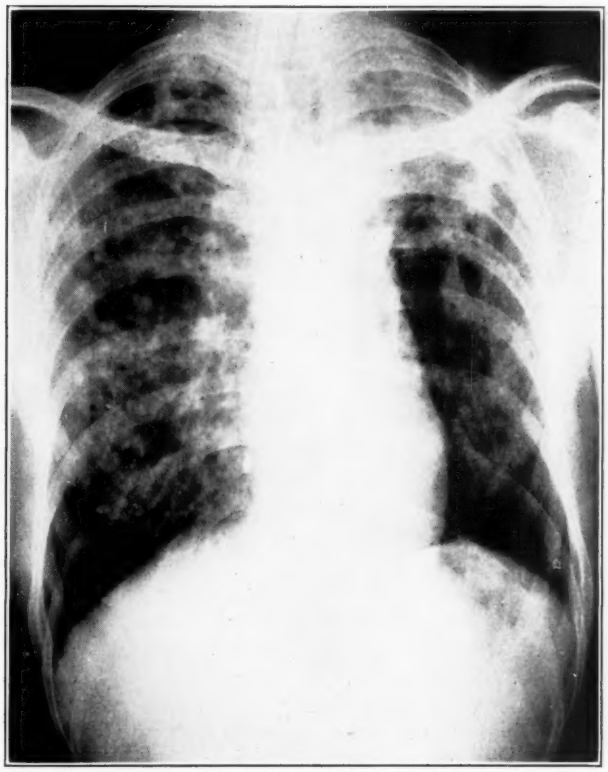

Fig. 2.—Tuberculosis of stomach; preoperative chest x-ray.

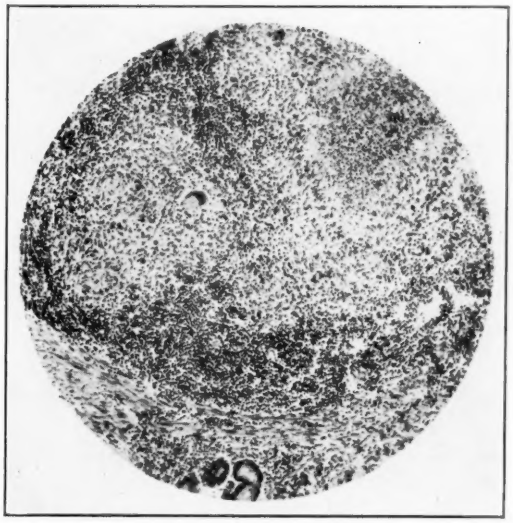

Fig. 3.—Tuberculosis of stomach wall, showing typical giant cell formation (×65).

upper portions of both lungs since the examination preliminary to operation. Against advice, however, the patient left the hospital July 24. He died at home Aug. 21, 1936, of pulmonary tuberculosis.

Pathologic examination of the excised prepyloric portion of the stomach, made by Dr. Newton Evans, follows: "The specimen consists of the wall of a hollow viscus, apparently the stomach, which has already been divided and now measures 15 by 7 cm. From the outer surface, a small amount of mesenteric or omental tissue projects. An indurated area on the serosal surface measuring 4.5 cm. in diameter presents large numbers of minute nodules having the appearance of miliary tubercles. In this area the wall is thickened and corresponds to a shallow ulcerated area in the mucosa, which has indistinct margins and is poorly differentiated from the surrounding mucosa. Section across this area shows the wall which measures 1.5 cm. in thickness to be filled with miliary sized tubercles.

Microscopic.—Section through this involved area shows that the ulcer on the inner surface is shallow and does not extend much beyond the depth of the muscularis mucosa at any point. The ulcer surface is largely covered by a necrotic area of tissue with a small amount of superficial exudate. Scattered through all the remaining layers of the stomach are numerous rounded discrete and conglomerate tubercles having the characteristic morphology, including great numbers of Langhan's type of giant cells, but with almost no areas of definite caseation. Acid-fast stain of the tissue sections reveals numerous acid-fast bacilli having the typical morphology of tubercle bacilli. These are found within the tubercles, occasionally within the giant cells, and in considerable numbers in the granulation tissue immediately at the base of the necrotic ulcerated surface. No final conclusion can be reached as to the atrium of the infection in the stomach wall, but the impression is left that the infection probably began in the mucosa and extended through the lymphatics to all the tissue layers of the involved area of stomach wall.

Diagnosis.—Tuberculous ulcer and extensive miliary tuberculosis of the stomach wall."

SUMMARY

Tuberculosis does not attack the stomach very often, 211 definitely proved and quite probable cases having been reported to the end of 1937. To these is added a case in which a partial gastric resection was performed. The excised portion of the stomach wall contained an ulcer along with numerous miliary tubercles of typical structure, including giant cells and acid-fast bacilli. Pulmonary tuberculosis caused the patient's death four and one-half months after the operation.

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A CRITICAL SURVEY OF PERITONEOSCOPY

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PERITONEOSCOPY, the direct inspection of the abdominal cavity by means of an optical instrument, is not a new procedure, as the cystoscope has for many years been used for this purpose. However, with few exceptions, preliminary reports only of peritoneoscopy have been published and rarely followed by further publications. It is difficult to understand this lack of sustained interest in view of the satisfactory results and the safety with which this procedure can be carried out. Ruddock[1] again has reviewed the problem and described a new instrument which is more readily used than the cystoscope. His series of 500 cases, by far the most complete now available, has helped to recreate an interest in this subject. In this country Horan[2] and Benedict[3] recently have published series of fifty observations each, while Hope,[4] Anderson,[5] Findlay,[6] Stolze,[7] and others have issued preliminary reports.

Because of the diagnostic possibilities of peritoneoscopy, it was decided at the University Hospital to investigate its value and cases were carefully selected. All observations were carried out by one person so as to gain a uniform impression of the indications, technique, and results. During the past six months, peritoneoscopy rarely has been used as the preliminary study in this series, but it has been resorted to after inconclusive diagnosis had been made by other means, or when biopsy, or the operability of a clinically suspected neoplasm, was desired. The number of cases has greatly increased as the value and safety of peritoneoscopy have been demonstrated. It has come to be considered a valuable final authority in diagnosis, equal in many instances to laparotomy and having only a fraction of the expense or morbidity of a major operation.

TECHNIQUE

The technique used is essentially that described by Ruddock[1, 8] and subsequently by many others. The instrument set used was illustrated in his article and is now known as the Ruddock peritoneoscope. Patients are prepared as for laparotomy and all examinations are carried out aseptically. We have found that an enema followed by 1 c.c. of pitressin (Horan[2]) aids greatly in reducing intestinal volume, thus allowing more room for observation. Morphine sulfate was the only sedative used. One per cent procaine local anesthesia was used in all but one instance, the

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second. This patient complained so bitterly of pain during the movement of the instrument that gas anesthesia was used. In retrospect, it is apparent that only the site of puncture was anesthetized. Since then local infiltration has been carried to all layers in an area of 6 to 10 cm. from the puncture site. This has allowed greater distention of the abdomen and painless manipulation of the instrument. The incision has generally been placed in the rectus muscle at the level of the umbilicus, although this has varied according to local pathology. A nick in the fascia is routinely made to facilitate the introduction of the large trocar. Room air of an unknown quantity and pressure is used for the pneumoperitoneum. No respiratory difficulties were encountered, although overdistention was occasionally accompanied by nausea. Observation was successful in all instances but occasionally was limited by adhesions, particularly in those patients who had undergone previous surgery. Considerable skill can be attained in maneuvering in and out among adhesions. Walls of adhesions too long to circumvent can be pierced and observation carried beyond. We have never attempted to cut adhesions as a therapeutic measure. In no case was it necessary to re-examine a patient because of inadequate observations.

Shifting the patient's position will frequently help to visualize the superior surface of the liver or pelvis. Transillumination of the stomach has not been uniformly successful. It has been helpful to distend the stomach with air by means of the Rehfuss tube. Peristalsis is thus initiated and its course through the stomach observed. The duodenum is brought into relief and is fairly well visualized by this distention. We have not used cystoscopy or sigmoidoscopy in conjunction with our examinations as suggested by Ruddock. After the initial 10 cases, biopsy was attempted whenever indicated. Of the 14 cases in which the clinicians desired biopsy, we were able to do so in 12. Failures were in liver biopsies where tissue taken for examination was inadequate or too mutilated. After preliminary cauterization of overlying blood vessels, it has been found feasible to obtain bits of mesenteric lymph node. A uniform plan of observation was followed, beginning in the right upper quadrant and passing around in a clockwise direction. Complete examinations were done in all cases. Unless enlarged, the spleen was seldom seen and the appendix was rarely found.

COMPLICATIONS

To date there has been no mortality or morbidity. Patients not confined to bed by the primary disease have been allowed up on the same or the following day. Three have complained of transitory shoulder pain. A hematoma has occurred in the wounds of two deeply jaundiced patients. One woman with a six-inch panniculus and uncontrolled diabetes mellitus suffered a minor wound necrosis. Thus far we have

not been forced to laparotomy either by bowel perforation or by hemorrhage, but it is undoubtedly only a matter of further experience before this occurs.

ACCURACY OF DIAGNOSIS

Based on this particular series it is impossible to draw numerical conclusions concerning the accuracy of diagnosis by peritoneoscopy compared to the clinical acumen of the hospital at large. In one large group of cases the clinical impression was fairly certain and peritoneoscopy served only to confirm the diagnosis, secure a biopsy, or estimate operability. Had peritoneoscopy alone been employed, one cannot say how accurate it might have been. In another large group of cases complete clinical studies had failed to reach a conclusive diagnosis, although supplying negative information. Peritoneoscopy was expected to select the proper diagnosis from an array of clinical possibilities presented by a large teaching staff. Obviously some clinicial would be correct, although no one clinician could afford to be certain. Peritoneoscopy settled the diagnostic problems in these situations in a high percentage of cases.

DISCUSSION OF CASES

Only cases that had been thoroughly studied by other means were accepted for peritoneoscopy, although, as its value has been demonstrated, it has occasionally been used as a short cut to diagnosis. No patient whose condition did not offer a definite question for answer was examined. With the indication for peritoneoscopy as a classification, the cases may be divided into the following general groups:

I. Liver-spleen syndromics: Includes biliary tract pathology, primary liver disease, and enlargements of both liver and spleen of unknown etiology.

II. Suspected abdominal malignancies: These were clinically diagnosed as malignancies, but confirmatory biopsies were desired, or the primary site or operability was questioned.

III. Identification of unknown masses in the abdomen.

IV. Ascites of unknown origin.

V. Tuberculous peritonitis.

We have not been asked to diagnose ectopic pregnancy nor to see many patients for other gynecologic complaints. As cautioned by Ruddock, we have avoided all acute abdomens.

Group I. Liver-Spleen Syndromics (15 Cases) (Table I).—Clinical diagnosis in the problem of jaundice or of hepatosplenomegaly rarely can be accurate, but it must be obtained to guide rational treatment. Peritoneoscopy, with none of the dangers of laparotomy, gave an accurate working diagnosis in 14 cases. In the fifteenth (Case 2) an early carcinoma at the head of the pancreas was diagnosed as a common duct stone and laparotomy was advised. This advice was not followed as

TABLE I

LIVER-SPLEEN SYNDROMES

CASE NUMBER	CLINICAL DIAGNOSIS	INDICATION FOR PERITONEOSCOPY	DIAGNOSIS BY PERITONEOSCOPY	BIOPSY	SUBSEQUENT COURSE
1 No. 365469	Jaundice, carcinoma, or common duct stone	Etiology of jaundice	Carcinoma at head of pancreas, no liver metastases	Adenocarcinoma, metastatic from breast	Previous radical mastectomy, no local recurrence; death, 6 weeks
2 No. 417742	Jaundice, carcinoma, or common duct stone	Etiology of jaundice	No carcinoma, probably common duct stones	None	Autopsy: small carcinoma at ampulla of Vater, no metastases
3 No. 414175	Jaundice, carcinoma at head of pancreas	Etiology of jaundice	Cirrhosis of liver, no cholecystitis	None	Cholecystectomy, normal gallbladder, liver biopsy, atrophic cirrhosis
4 No. 297271	Catarrhal jaundice or cirrhosis	Etiology of jaundice	Cirrhosis of liver, chronic cholecystitis	None	Cholecystectomy, ulcerative cholecystitis; liver biopsy, severe portal cirrhosis
5 No. 425525	Jaundice, carcinoma at head of pancreas	Etiology of jaundice	Carcinoma at head of pancreas	From liver, carcinoma	Cholecystgastrostomy
6 No. 419394	Jaundice, cirrhosis, or malignancy	Etiology of jaundice	Normal liver and gall bladder, catarrhal jaundice	None	Clinical course and subsequent x-ray; confirm diagnosis four months later
7 No. 421344	Jaundice, generalized carcinomatosis	Etiology of jaundice (?) primary	Cirrhosis with ascites, no malignancy	None	Improved with medical regime three months later
8 No. 415782	Jaundice, hepatosplenomegaly	Etiology of jaundice	Biliary obstruction, no cirrhosis or malignancy	None	Stricture of common duct; hepatosplenomegaly reduced with common duct drainage
9 No. 398184	Cirrhosis with ascites	Diagnosis	No ascites, no cirrhosis	None	Elective herniorrhaphy three months later
10 No. 418132	Hepatomegaly, no jaundice	Etiology of hepatomegaly	Metastatic malignancy (?) from head of pancreas	Adenocarcinoma mucosum in liver	Primary undetermined
11 No. 137681	Hepatomegaly	Etiology of hepatomegaly	No hepatomegaly, large inflammatory mass in right upper quadrant	None	Carcinoma of gall bladder; no metastases; large abscess
12 No. 171650	Hepatomegaly (?) gumma	Diagnosis	Large neoplasm in liver	None	No further information as yet
13 No. 419432	Hepatosplenomegaly (?) Banti's disease	Diagnosis biopsy	Cirrhosis of liver, chronic cholecystitis	Unsuccessful	Cholecystectomy; chronic cholecystitis; biopsy, atrophic cirrhosis
14 No. 419922	Hepatosplenomegaly	Etiology of hepatomegaly	Metastatic carcinoma (?) from head of pancreas	Inadequate from liver	Primary undetermined
15 No. 420998	Splenomegaly	Etiology of splenomegaly	Severe toxic hepatitis with splenomegaly	Inadequate from liver	Splenectomy, anemia infarcts; liver biopsy, atrophic cirrhosis

the patient died. The patient's course would not have been adversely affected, had he lived, because of the erroneous diagnosis. Lesions at the head of the pancreas can only be seen peritoneoscopically if they are far enough advanced to have metastasized or to have pushed up from the retroperitoneal spaces. However, the liver and gall bladder can be readily inspected and an intelligent correlation of what is seen, we believe, will give the correct answer. In contrast to this one mistaken diagnosis made by peritoneoscopy, clinical diagnoses were wrong in three instances. The subsequent course of these three patients was altered by the change in diagnosis: Case 7 received treatment for cirrhosis with ascites rather than palliation for abdominal carcinomatosis; Case 6 was saved from laparotomy; and Case 9 had an elective herniorrhaphy after the clinical diagnosis of cirrhosis with ascites was corrected.

Laparotomy was the last recourse to establish a positive diagnosis in all 15 cases. This major operation was eliminated in 7 of the 15 cases. In an eighth, laparotomy was not advised but was done because of lack of confidence in the peritoneoscopic diagnosis. Surgery was carried out in the remaining 6 cases as suggested and was found to be the procedure of choice.

We feel from our brief experience that peritoneoscopy accurately answers the diagnostic problem and indicates the therapeutic approach in jaundice and in hepatosplenomegalies.

Group II. Suspected Abdominal Malignancies (17 Cases) (Table II).— Eight of these were carcinoma of the stomach, a small percentage of the total gastric malignancies seen in University Hospital during this six months' period. More gastric neoplasms were not examined because of lack of confidence in peritoneoscopy. We have never felt that clinical findings alone could accurately disclose the inoperable carcinoma of the stomach but we now know that peritoneoscopy can save many of these patients from operation. Therefore, we feel that peritoneoscopy should be done on all gastric neoplasms. The borderline cases will always come to operation. Three of the 8 patients with carcinoma of the stomach were saved from operation, but only 2 of the 5 considered operable were submitted to gastric resection.

Eight of the remaining 9 cases in this series were considered clinically to have abdominal malignancies. The ninth was a case of proved carcinoma of the rectum with a question of metastases to the liver, which were found by peritoneoscopy. Routine peritoneoscopy was considered for the large group of rectal neoplasms seen at the University Hospital, but this was rejected because the majority of these cases, whether operable or not, require a colostomy. Clinical diagnosis of abdominal malignancy in 5 of the 8 cases was established. Two had no malignancy at all and 1, by peritoneoscopy, was thought to have an operable carcinoma of the ovary, which at operation was found to be endometriosis of the tube and ovary. Peritoneoscopic examination, although mistaken in the

TABLE II

ABDOMINAL MALIGNANCIES

CASE NUMBER	CLINICAL DIAGNOSIS	INDICATION FOR PERITONEOSCOPY	DIAGNOSIS BY PERITONEOSCOPY	BIOPSY	SUBSEQUENT COURSE
16 No. 423641	Carcinoma of stomach	(?) Operability	Operable	None	Laparotomy: carcinoma too high on lesser curvature
17 No. 419893	Carcinoma of stomach	(?) Operability	Inoperable due to local extension	Adenocarcinoma	Death three weeks later
18 No. 416773	Carcinoma of stomach	(?) Operability	Inoperable due to local extension	None	Slowly down hill
19 No. 422457	Carcinoma of stomach	(?) Operability	Inoperable due to local extension	Carcinoma	No further information
20 No. 424370	Carcinoma of stomach	(?) Operability	No metastases but locally extensive lesion	None	Laparotomy; not resectable
21 No. 424888	Carcinoma of stomach	(?) Operability	Operable	None	Gastric resection
22 No. 424574	Krukenberg tumor	Confirm diagnosis	No malignancy in pelvis, (?) the malignancy in the stomach	None	Laparotomy, no pelvic neoplasm, gastric resection neurofibroma
23 No. 417303	Previous excision of malignant ulcer	(?) Recurrence of gastric neoplasm	No metastases, considered operable	None	Inoperable due to involvement of posterior wall of stomach
24 No. 425318	Proved carcinoma of rectum	(?) Abdominal metastases	Metastases to liver	None	Transverse colostomy only
25 No. 419415	Carcinomatosis (?), origin in pelvis	Diagnosis biopsy	Carcinoma of right ovary	Cystadenocarcinoma	Palliative x-ray therapy
26 No. 411798	Carcinomatosis (?), origin in pelvis	Diagnosis biopsy	Carcinoma of left ovary	Carcinoma	Failing rapidly
27 No. 408257	Ascites (?), recurrent carcinoma of the stomach	Diagnosis	Abdominal carcinomatosis	None	Death three weeks later
28 No. 421510	Generalized carcinomatosis	(?) Origin	Abdominal carcinomatosis (?) origin in retroperitoneal mass	None	No further information
29 No. 423045	Abdominal carcinomatosis	(?) Origin	Abdominal carcinomatosis arising at head of pancreas	Unsatisfactory from liver	Autopsy: carcinoma, primary in terminal ileum
30 No. 424077	Carcinomatosis (?), origin in pelvis	Diagnosis	Negative abdomen, chronic pelvic inflammation	None	Discharged on conservative regime
31 No. 420540	Obesity (?), pelvic neoplasm	Diagnosis, (?) operability	No malignancy, fibroid uterus, cystic ovary	None	No change three months later
32 No. 335824	(?) Pelvic neoplasm	Diagnosis, (?) operability	Carcinoma of right ovary, operable	None	Laparotomy: endometriosis of tube and ovary

diagnosis in the last case mentioned, indicated the proper therapeutic approach in all 8. The clinical impression was definitely in error in the two cases shown not to have malignancy. Although previously laparotomy would have been necessary to gain the above information in all 9 cases, it probably would not have been carried out in 2 of the advanced malignancies.

We have concluded from this small group of 17 cases of abdominal malignancy that peritoneoscopy can save many patients from operation by eliminating the inoperable carcinoma of the stomach, establishing the diagnosis of abdominal carcinomatosis, and evaluating the extent of pelvic neoplasms. Treatment can be logically planned with the information thus gained by peritoneoscopy.

Group III. Identification of Unknown Masses in the Abdomen (Table III).—The clinically described mass was identified with certainty in only 6 of the 11 cases. In a case of testicular tumor it was quite certain that there was no abdominal mass as felt clinically. In the remaining 4 no accurate diagnosis could be made by peritoneoscopic findings because of the retroperitoneal position of the masses. Three of these 4 subsequently came to operation.

Three of the 11 would never have come to operation. Peritoneoscopy was used to identify retroperitoneal masses in 2 for whom surgery was not indicated; in the third it was used as a diagnostic shortcut, hardly the method of choice, to diagnose a hypernephroma, which was a clinical diagnostic error.

Laparotomy was probably inevitable in 8 of the 11 cases. It was eliminated in 2 because of carcinomatosis. Of the 6 operated upon, surgery had been correctly advised by peritoneoscopic examination in 5 but with only 3 correct diagnoses. In the sixth case no abdominal mass and no surgical lesion were found, a clinical and surgical error.

We feel that peritoneoscopy will do little to identify retroperitoneal masses. It will aid in locating intra-abdominal masses and will eliminate laparatomy in those having advanced abdominal malignancy. Therefore this examination for unidentified abdominal masses must be recommended with reservations.

Group IV. Ascites of Unknown Origin, 3 Cases (Table IV).—Biopsy by peritoneoscopy proved carcinomatosis in 2 cases and in the third an accurate diagnosis was not made. Three months later autopsy showed an intrahepatic neoplasm in this third case. With thorough clinical studies before peritoneoscopy, this group of ascites of unknown origin will continue to be small, but peritoneoscopy may be expected to give the correct diagnosis.

Group V. Tuberculous Peritonitis, 4 Cases (Table V).—The diagnosis of well-advanced tuberculous peritonitis was established by peritoneoscopy by 2 cases. The other 2 patients presented vague abdominal complaints with clinical diagnosis of intestinal or peritoneal tuberculosis.

TABLE III

ABDOMINAL MASSES

CASE NUMBER	CLINICAL DIAGNOSIS	INDICATIONS FOR PERITONEOSCOPY	DIAGNOSIS BY PERITONEOSCOPY	BIOPSY	SUBSEQUENT COURSE
33 No. 419002	Mass in right midepigastrium	Identification of mass	Negative except for (?) mass about duodenum	None	Laparotomy: carcinoma at head of pancreas without metastases
34 No. 419822	Mass in right upper quadrant	Identification of mass	Chronic cholecystitis, no carcinoma	None	Laparotomy: chronic cholecystitis and lithiasis
35 No. 422481	Mass in right upper quadrant, postoperative cholecystectomy	Identification of mass	No carcinoma (?) mass at head of pancreas	None	Laparotomy: adhesions only from previous surgery
36 No. 423560	Mass in right upper quadrant	Identification of mass	No carcinoma, chronic cholecystitis	None	Laparotomy: chronic cholecystitis and lithiasis
37 No. 419642	Retroperitoneal sarcoma	Identification of mass in epigastrium	Retroperitoneal mass without metastases	None	Laparotomy: carcinoma of cardia of stomach
38 No. 417310	Mass extrinsic to stomach	Identification of mass	Inoperable carcinoma of stomach	None	Death three weeks later
39 No. 422004	Mass epigastrium, (?) neoplasm in lungs	Identification of mass, (?) carcinomatosis	No carcinomatosis, mass near body of pancreas	None	No further information from other studies
40 No. 420672	Large mass in right abdomen	Identification of mass, (?) carcinomatosis	Hypernephroma	None	Pyelograms positive; peritoneoscopy used as a diagnostic short cut
41 No. 417413	Low abdominal mass, (?) carcinoma from ovary	Biopsy, identification of mass	Pelvic abscess, no malignancy	None	Laparotomy; pelvic abscess
42 No. 410671	Midabdominal mass, (?) carcinoma from ovary	Identification of mass	Carcinomatosis arising in right ovary	From peritoneum, adenocarcinoma	Palliative x-ray therapy
43 No. 400404	Postoperative tumor of the testicle	Abdominal mass or metastases	No abdominal mass, no liver metastases	None	No further treatment, but to be observed

TABLE IV

ASCITES

CASE NUMBER	CLINICAL DIAGNOSIS	INDICATION FOR PERITONEOSCOPY	DIAGNOSIS BY PERITONEOSCOPY	BIOPSY	SUBSEQUENT COURSE
44 No. 415162	Ascites	Etiology of ascites	(?) Syphilitic hepatitis, no malignancy	None	Autopsy: carcinoma of large bile ducts, no metastases except deep in liver
45 No. 422732	Ascites, mass in left upper quadrant	Etiology of ascites	Abdomen full of mucin from an adenocarcinoma mucosum	Mucin from adenocarcinoma mucosum	Peritoneoscopy used as the initial and only study
46 No. 331846	Ascites; 3 years postoperative radical breast	Etiology of ascites, (?) carcinomatosis	Carcinomatosis of peritoneum only	Diffuse carcinomatosis	Death three months later

TABLE V

ABDOMINAL TUBERCULOSIS

CASE NUMBER	CLINICAL DIAGNOSIS	INDICATION FOR PERITONEOSCOPY	DIAGNOSIS BY PERITONEOSCOPY	BIOPSY	SUBSEQUENT COURSE
47 No. 413591	Pelvic tuberculosis	Diagnosis	Pelvic tuberculosis	None	Guinea pig negative; still in Sanatorium
48 No. 422757	Tuberculous peritonitis	Diagnosis	Peritoneal tuberculosis; generalized; no adhesions	Active tuberculosis	Smears and cultures negative
49 No. 413229	Tuberculous peritonitis, operative diagnosis elsewhere	Diagnosis	Negative abdomen	Negative mesenteric lymph gland	Continues to have vague abdominal distress
50 No. 351749	Postoperative thoracoplasties, (?) intestinal tuberculosis	Diagnosis	Negative abdomen	None	Continues to have same vague abdominal complaints

In neither of these 2 could the diagnosis be confirmed. We hope to be able to re-examine the 2 patients of proved tuberculous peritonitis at intervals as much may be learned of the disease in this manner.

SUMMARY

Peritoneoscopy has been done on fifty patients. The cases are reported herein in detail as a critical survey of this method of examination. We have found it to be entirely safe and very accurate, supplying much of the information usually gained by laparotomy, with none of the expense or morbidity of a major operation. Satisfactory biopsies may be obtained with little additional risk to the patient.

Peritoneoscopy will give an accurate diagnosis and indicate the treatment in cases of jaundice and hepatosplenomegaly. It should be used routinely in carcinoma of the stomach to avert operation in the inoperable cases. The extent of pelvic and abdominal neoplasms can be accurately estimated for proper treatment. It cannot be expected to identify retroperitoneal masses unless they are far advanced. Abdominal tuberculosis can be readily diagnosed and its course should be followed by repeated peritoneoscopic examinations. Many patients with a presumptive clinical diagnosis which would contraindicate operation can be safely examined by peritoneoscopy and receive the benefit of treatment based on correct diagnosis. These diagnoses may be at variance with the clinical diagnoses and may change the prognosis entirely.

In short, we feel that every large teaching hospital should have one of these instruments for diagnostic studies.

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TECHNIQUE OF THE INJECTION TREATMENT FOR INGUINAL HERNIA

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IT IS a long time since Billroth prophesied that if a solution could be perfected which would cause the proliferation of connective tissue when injected into the inguinal canal, then the treatment of hernia in a large measure would be simplified. This prophesy is being fulfilled. Solutions have been evolved which produce sclerosis in a safe manner, as described by one of us (H. I. B.) in a previous article.[1] This is not sufficient, however, to place this therapy on a firm footing. It is important, in addition, to develop a sound technique in order to make the method efficient and enduring.

It will serve no purpose to repeat the historical summaries of previous writers. Most of this work has been repetitious, as pointed out by Crohn.[2] For those who are interested in the chronological growth of this method, we have arranged a chart, Table I. This historical summary shows that the method has been in use for practically one hundred years. It has waxed and waned in popularity during the past century depending upon the character of the men into whose hands it fell. A more favorable background has been developed recently, as a result of important histological studies[3-6] and improved solutions. The important point at the present time is that there is still room for improvement in technique. It is the purpose of this paper to describe an injection method which is based upon sound principles.

A review of the literature shows a lack of interest in detailed or standardized technique. Those authors who mention technique do so in a general way and favor angles of injection that seem to the authors essentially unsafe. The entire crux of the problem lies in the proper conception of what takes place with injection therapy. What is aimed at is adhesion between important structures as the result of fibrous tissue growth. This fibrous proliferation following chemical irritation is a definite fact which has been proved and confirmed by previous workers. It must be emphasized that the object is not scar tissue as such, because it is perfectly possible to create huge lumps of dense fibrous tissue and get a complete failure. What is aimed at, rather, is permanent adhesion of weakened to relatively normal structures as the result of fibrous union. It is, therefore, of the utmost importance to place the needle point in the proper fascial plane by a definite orderly and sys-

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TABLE I

DATE	AUTHOR	NO. OF CASES	SOLUTIONS USED	METHOD AND RESULTS
1835	Velpeau[3]	3	Iodine	Flushed hernial sac through incision in scrotum; all 3 cases cured
1836	Pancoast[4]	13 in 8 yr.	Lugol's solution. Tr. cantharides	Used syringe and cannula; all cured
1840	Jaynne[5]		Essential oils. Tr. cantharides	Special patented instrument; claimed 75 per cent cures
1841	Heaton[6]		Secret at first. Solution quercus albus	Special syringe and needle; disfavor of American colleges due to secrecy of method; claimed too much (100 per cent cures [?]); only one injection given; patient put to bed and bandage applied
1877	Schwalbe[7]		70 per cent alcohol	Daily injections for about two weeks; patient kept in bed
1881	Warren[8]		Quercus albus	Disciple of Heaton; only one massive dose given and patient confined to bed; first to describe rationale of seroplastic tissue repair; recommended painting inguinal rings and canal with solution during surgical operation (80 to 85 per cent cures)
1892	Marcy[9]			Discussed injection treatment in monograph on hernia
1893	Manley[10]			Emphasized proper selection of cases
1900	Pina Mestre[11]	15,000 (20 yr.)	Pina Mestre	Claims inguinal closed in 10 to 15 days (98 per cent cures)
1900 to 1932	Mayer[12]	21,000 (30 yr.)	Zinc sulph. phenol and alcohol	First to make treatment ambulant; 98 per cent cures; 2 per cent cured subsequently; small doses; patient wore truss during treatment
1904	Wollerman[13]	554	Alcohol (?)	92 per cent cure
1907	Lannelongue[14]		10 per cent zinc chloride	Very enthusiastic about its use in hernia injection after noting its effect on stimulating growth of fibrous tissue in tuberculous deposits
1928	Steffen[15]	2,775 (30 yr.)	Alcohol	One injection weekly for 1 year; no deaths in 30 years of treatment (91.2 per cent cures)
1929	Wyss[16]	Review of 4,632	Alcohol	3,084 follow-ups; 91 per cent cures; no vital damage; 4 per cent complications (abscess, orchitis, hydrocele, atrophy of testis)
1929	Hall[17]	33	Pina Mestre	Histologic work on animals (peritoneal injections); formation of adhesions and a connective tissue barrier, thus effectively blocking and obliterating the canal; 1 failure

TABLE I—CONT'D

DATE	AUTHOR	NO. OF CASES	SOLUTIONS USED	METHOD AND RESULTS
1930	Goldbahn[18]		Alcohol	Reported results of unskilled injections in cases of strangulated irreducible hernias, resulting in sepsis, fecal fistulas, and deaths
1930	Jameson and Cantala[19]	64	Pina Mestre	12 to 15 daily injections; claim it is the method of choice in cases of recurrent hernia
1931	Wolfe[20]	22	Pina Mestre	Described seroplastic exudation and formation of adhesions in inguinal canal; injected into peritoneum of animals and produced plastic peritonitis; claimed vas not injured if cord injected
1932	La Rochelle[21]		Pina Mestre	Injections should supplement operative treatment, help produce internal tissue pad or truss
1933	McKinney[22]		Phenol, alcohol, oil of thuja	Production of fibroblasts (without necrosis) in adjoining muscle tissue
1934	Larson[23]	137	Phenol, alcohol, and thuja solution	8 injections; injection treatment suitable in 90 per cent of cases seen (93.5 per cent cures); no serious complication
1934	Gray[24]	20	Mayer's solution	75 per cent cure
1934	Bratrud[25]	406	Tannic solution	4 per cent recurrences with three final failures; animal injections; marked fibroblast proliferation, no polymorphonuclears, giant cells, or necrosis
1934	Rice[26]	600	Phenol, alcohol, and oil of thuja, sodium psylliate	2 failures; no severe complications; histologic work on biopsy specimens from injected cases at operation shows dense adult fibrous tissue present by the forty-second day after injection
1935	Fowler[27]	700 (5 yr.)	Tannic and gallic acids	98 per cent cure, no serious complications; advised initial overbuilding of tissue to allow for absorption
1935	Fantus[28]			Believes certain percentage of reducible hernia curable by injection
1935	Quillin[29]	242		210 indirect, 4 direct, 23 recurrent, 5 umbilical; work and investigation on cadaver
1935	Kretzschmar[30]	140		Points out infections close hernial sac same as nature closes processus vaginalis
1936	McMillan[31]	400	Thuja solution, tannic acid	8 per cent recurrences; no serious complications
1936	Zieman and Larkowski[32]	1	Tr. of thuja	Report necrosis of cord structures with swelling of vas after one injection

TABLE I—CONT'D

DATE	AUTHOR	NO. OF CASES	SOLUTIONS USED	METHOD AND RESULTS
1936	Girard[33]	174	Tannic acid, phenol, and alcohol; thuja solution; sylnasol, Pina Mestre	Series included 19 postoperative recurrences; also injected postoperative repairs with threatened weakening; claims recurrences in injected cases due to undertreatment
1936	Gordon and Gordon[34]	5		Contraindication of injection treatment in sliding hernia; present in 1.2-1.5 per cent of cases seen; injections, however, do not interfere with operative procedure or result
1937	Crohn[2]		Phenol, alcohol, and oil of thuja	Confirmed Rice's histologic work; no serious complications
1937	Rea[35]			Reviewed 75 cases injected for unilateral inguinal hernia and found only one case of delay in libido; followed 26 cases injected for bilateral inguinal hernia for 3 years and found normal spermatic count; no sterility

tematic plan. At the completion of the case a line of adhesions will be formed in much the same manner as after a thorough surgical operation.

The points of adhesion that are produced by this method are not completely understood. From the few operative reports presented in the literature,[34] and from our personal clinical observations, it would seem that one point of adhesion is between the aponeurosis of the external oblique and the underlying internal oblique muscle. There is evidence at hand to show adhesions between conjoined tendon and the overlying fascia of the spermatic cord and external oblique muscle. There are other points of adhesion following this treatment which resemble largely those following operative methods. However, much work is necessary before more definite statements can be made. It may be pointed out in general that the adhesions aimed at involve fascial structures, because it has been shown recently[37] that adhesions of fascia to muscle are at best temporary and evanescent.

In studying the evolution of the modern operation for inguinal hernia, one is impressed by the multiplicity of procedures which have been and are still being used. It is evident from this that no single method is without criticism. More important still, the trend of the new operations points out clearly the defects inherent in the older surgical approach. The operative treatment of hernia has been taken for granted by the majority of the profession in the past. For a long time no proper study was made of the permanent planes of adhesion following surgical repair. Other problems in connection with the etiology and recurrence of hernias have not been solved. The mechanics of the musculofascial

supports have never been clearly understood. The sphincterlike mechanism at the external ring has not been clearly elaborated. It has remained for the injection treatment of hernia to stimulate interest on these important points and lead the way for more rational therapy by both methods in the future.

Concretely, in comparing modern injection therapy with the latest endofascial approach,[38] one is impressed by the fact that both procedures aim at the same end result. In view of the fact that both methods produce adhesions in identical planes between similar structures, it may be concluded that theoretically, in properly selected cases, the injection method is superior to the operative procedure. The open technique involves division of fascia, muscle, nerves, and blood vessels and must weaken structures which are not normal to begin with.

Before attempting to do injection therapy, one should acquaint himself with the detailed anatomy of the inguinal region. This can only be done by repeated cadaver injection and dissection. Study of dye injection and minute anatomy of the canal itself forcibly emphasizes the fact that important structures are only fractions of centimeters away from the needle point. None of the techniques previously published have taken into account these dangers. The method to be outlined recognizes the hazards involved and the injection angles it describes are the safest ones that accomplish the desired result. The basic foundation of this technique rests upon the fact that a needle pointed toward the pubic spine will avoid most of the important structures in the inguinal region.

The manual dexterity acquired with the needle and syringe is indispensable and comes only after considerable clinical experience. Cadaver work, while essential, is only the preliminary phase of training, because the feel of the needle in dead tissue differs from that of the living. The best background for this special sclerosing technique is familiarity with injection treatment of varicose veins, hydrocele, and internal hemorrhoids.

Before leaving the subject of cadaver work, one should mention a rather interesting observation. It was noted that the colored fluid, although injected at one point of the inguinal canal, was found on dissection to have diffused over a wide area. This diffusion along the canal should not mislead the observer, because the spreading occurs only in one fascial plane and in all probability has very little action upon the fascia which lies either above or below it. For this reason, it is considered advisable in the actual injection to move the needle point so as to enter as many planes as possible during the treatment.

Careful study also brings out the fact that for permanent anchorage it is necessary to deposit irritating solutions not only in the canal itself but outside it. This is especially true in the case of direct hernia,

where one takes advantage of adhesions to the fascial insertions on the pubic bone. It can thus be seen that a good technique for the injection treatment of hernia must take into consideration numerous factors and it is not the simple procedure that previous authors have described.

TECHNIQUE

The equipment required is as follows: (1) Iodine, alcohol, applicators, gauze sponges and pads; (2) syringes: one 2 c.c. and one 5 c.c. glass syringe; (3) needles: 25 gauge 3/4-inch needles for anesthesia; 3- and 4-inch 20 gauge needles for deep injection; (4) solutions: 2 per cent procaine without adrenalin, sylnasol, monolate, proliferol, neogaltanol.

The patient is prepared for each injection by having him void so as to make certain the bladder is completely empty. The actual injection is performed with the patient lying supine and completely relaxed on a flat table. In this position the operator removes the truss and outlines the inguinal canal.

For practical purposes, the location of the inguinal canal is gauged by various means. Manual examination with one finger in the external ring is the simplest way. Noticing the shape of the bulge on cough is another means. Occasionally, the structures of the cord may be palpated for half the distance of the canal. In the spare subject, the course of the femoral artery and its branch, the deep epigastric, may be traced where it enters the internal ring. By the aid of all these factors, the inguinal canal may be mapped out with a fair degree of accuracy. The senior author's new method of studying the inguinal canal with the use of radiopaque solutions, which is reserved for a future paper, will probably prove to be the most exact manner of visualization.

INDIRECT HERNIA

The internal ring is usually first attached. The average location of this structure in the normal case has classically been described as one-half inch above the midpoint of a line drawn between the anterior superior spine and the pubic spine (Fig. 1). This is subject to individual variation and, in the presence of hernia, to considerable distortion. Therefore, in order to locate this structure, it is first necessary to outline the canal as previously described.

The actual injection of the internal ring is performed as follows: The location of the ring is marked with iodine. After preliminary skin anesthesia, the needle point is inserted approximately 1½ inches lateral to this point on the prolongation of a line running through the inguinal canal. The needle point is depressed so that it reaches the external oblique fascia slightly above the margin of the internal ring (Fig. 3) and, after penetrating the fascia, is continued in the same direction through the internal oblique muscle to the transversalis fascia. The

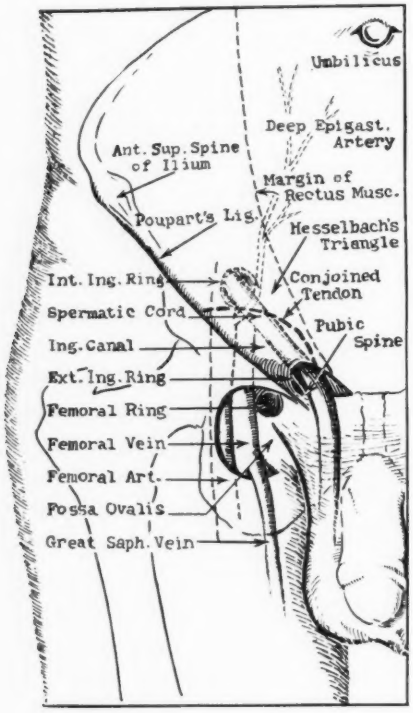

Fig. 1.

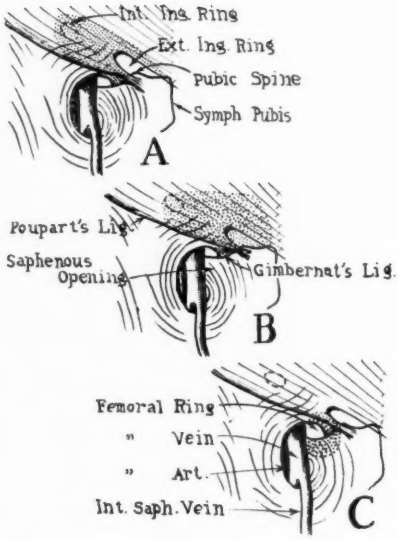

Fig. 2.

Fig. 1.—Surface markings.

Fig. 2.—Area injected in treatment of: *A*, indirect inguinal hernia; *B*, direct inguinal hernia; *C*, femoral hernia.

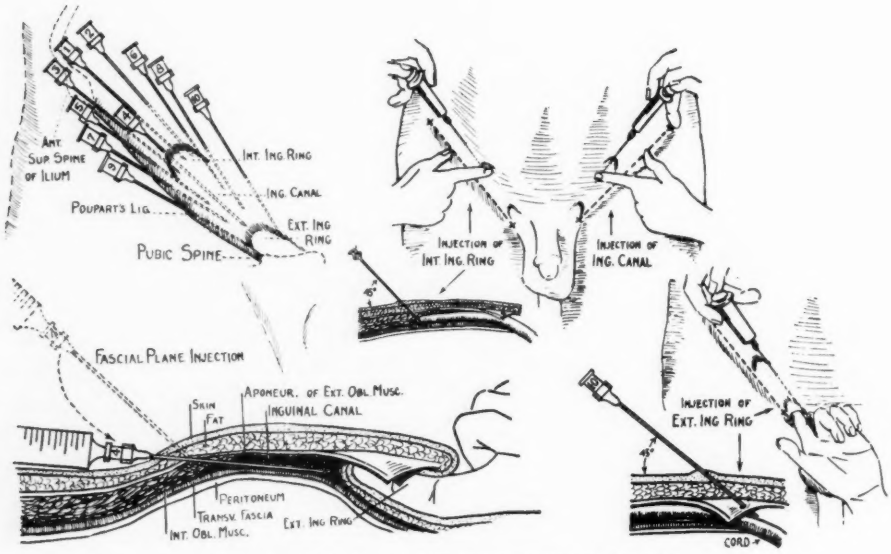

Fig. 3.—Injection of indirect inguinal hernia.

direction of the needle point, as in subsequent injections, is toward the pubic spine and the angle that the needle makes with the inguinal canal is approximately 45°. For practical purposes, it is sufficient to obtain this angle with the skin, although in doing so one must consider the degree of obesity present. The feeling experienced in transversing the structures between the skin and the transversalis fascia is characteristic to the experienced touch. The first pronounced sensation is the "jump" of the needle point in going through the aponeurosis of the external oblique. This sensation varies in different patients, depending upon the degree of firmness of the fascial structure. There is a definite lack of resistance comparable with the successful entry of the spinal canal during a lumbar tap.

Having reached the plane of transversalis fascia, the syringe is depressed and the needle point carried down further in the direction of the pubic spine until the region of the internal ring is reached. With the standard 3-inch needle, starting the injection 1½ inches above the internal ring, the needle will penetrate about 2½ inches of tissue before the internal ring is reached. One should always attempt to follow the needle point in its voyage by palpation with the opposite hand. In the thin subject it is often possible to feel it throughout the entire procedure. This is aided by depressing the syringe from time to time.

The second and third injections are given in the same region (Fig. 3, *2*, *3*), attempting to reach the medial and lateral borders of the ring. Occasionally some of the solution will diffuse toward the internal oblique muscle to cause swelling above the canal the following day. This reaction subsides promptly, but the symptoms may cause apprehension on the part of the patient unless he is warned beforehand.

The fourth injection is started about ¾ inch above the internal ring and the needle point carried through the external oblique aponeurosis and the muscles beneath it. Then the syringe is depressed and the needle carried through the canal to the external ring where it is palpated by the examining finger which has invaginated the scrotum. The solution is deposited as the needle is withdrawn, so that the entire canal is bathed.

With every injection, it is advisable to aspirate first to make certain that no blood vessel has been entered. Following this, a few minims of solution are injected and the resulting symptoms noted. After a lapse of three or five minutes, if no cramplike peritoneal symptoms are complained of, the remainder of the solution is slowly deposited.

The fifth, sixth, seventh, and eighth injections are made, as noted on the diagram, in the midcanal area (Fig. 3). In this region the roof is composed mainly of external oblique aponeurosis. This makes the injection a very simple procedure, the only caution to be observed being

avoidance of the cord. With the fifth and seventh injections, Poupart's ligament should be injected so as to favor adhesions to this important stable supporting structure.

The general angle of all the preceding injections is the same and the needle point is always carried toward the pubic spine. This makes for what may be called the angle of safety. Our cadaver work has convinced us that no other approach is as safe, and clinical experience has confirmed our observations.

The injection of the external ring is comparatively simple. For this procedure, it is always advisable to keep the examining finger in the ring itself. The crura are injected separately (ninth and tenth injections) and the needle point carried through the spermatic fascia, so that, on withdrawal of the syringe, the various layers of fascia are successively infiltrated.

No case is ever complete without a few injections in the region of the conjoined tendon as described later. This is important to avoid a direct hernia which sometimes follows and often coexists.[39] The total number of injections varies with each case and with the type of solution used. The average number is fifteen but no case should be considered cured unless the inguinal canal is definitely fibrotic to the touch of the needle and all hernial impulse has been obliterated.

DIRECT HERNIA

There is an essential anatomical difference between the two types of inguinal hernia which forms the basis for the variation between the two techniques. In the indirect hernia the posterior wall of the inguinal canal is relatively intact. In direct hernia this structure is either weak or goes into the formation of the hernial opening (Fig. 4). In view of the fact that in the latter case there is nothing in the inguinal canal itself that can be considered a safe anchorage point, it is necessary to go outside of the canal to secure firm and lasting adhesions. Following the basic principle of anchoring weak to relatively secure tissue, in this type of hernia it is necessary to form adhesions between the conjoined tendon, transversalis fascia, and the ligaments attached to the pubic bone in that immediate region. Merley obliterating the inguinal canal itself, as has been recommended by other writers, is not sufficient to close this type of defect.

The technique for the injection of the upper half of the canal is exactly the same as in the indirect type. It is advisable to dispose of these injections early in the treatment so as to be able to concentrate on the region of the conjoined tendon. However, the obliteration of the upper half of the canal should not be neglected, even though it shows no apparent weakness, in order to prevent the development of an indirect hernia following the treatment. In those cases where the type of hernia

is not clear cut, or where a saddle-bag or combined type of hernia exists, the internal ring becomes an important consideration and is attacked with more emphasis.

Ordinarily, as illustrated in Fig. 5, the routine of injections is as follows: The first to fifth injections are performed in order to obliterate the upper half of the inguinal canal as described previously. The superior crus and the layers of the spermatic fascia are next infiltrated by the bimanual method (Figs. 3, *10* and 5, *6*). The cord is easily avoided. The inferior crus is then attacked. For this the invaginating finger is again used as a guide, the needle point being inserted over Poupart's ligament, 1½ inches lateral to the pubic spine. The layers of spermatic fascia and the aponeurosis forming the crus are infiltrated (Fig. 5, *7*).

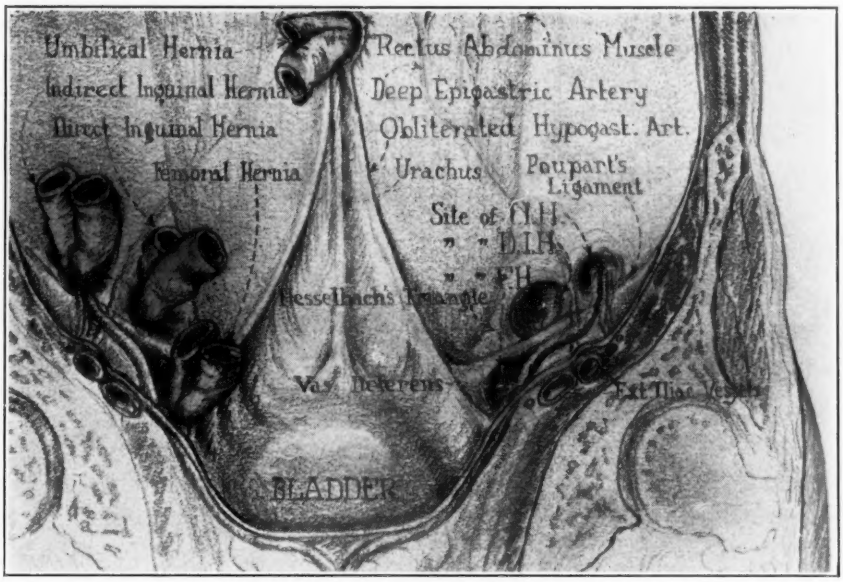

Fig. 4.—Anterior abdominal wall from within showing sites of umbilical inguinal and femoral hernias.

The important feature of the technique is the injection of the conjoined tendon. In order to perform this properly, the detailed anatomy of this structure must be known. Its condition should be ascertained at the outset of every case and one should note whether the tendon is displaced, thinned out, or not palpable. The rectus tendons must not be confused with the conjoined tendon. This is important because these two structures are attached closely together in the region of the pubic crest and pectineal line. Differential diagnosis is made by having the patient lie on his back, and, after placing the examining finger in the external ring, asking him to sit up. The opposite hand palpates the abdomen during this procedure and feels the contraction of the rectus muscles. The belly of the rectus muscle can be felt to tighten, and the muscle followed down to the tendon at its pubic insertion, where it is

also felt by the finger in the external ring. The conjoined tendon is more difficult to outline. However, in some cases, the edge is palpable. In others, the condition of the tendon itself can be made out as either firm or stretched. It is often possible to push the examining finger beyond the edge of the conjoined tendon against the transversalis fascia. In this position, the examining finger may be gripped tightly by a sphincter-like mechanism as the patient is asked to sit up.

In injecting this important structure, the needle is started at a point 1½ inches lateral and superior to the pubic spine, keeping the syringe parallel with the lateral border of the rectus muscle. The needle is aimed at the pubic spine. The point pierces successively the skin, superficial fascia, external oblique aponeurosis, conjoined tendon, and is arrested by the pubic spine (Fig. 5, *9*). The needle is now withdrawn

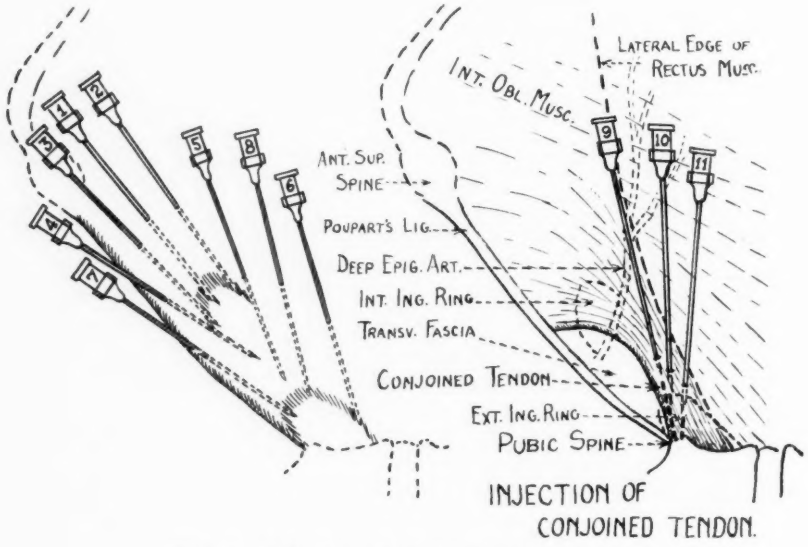

Fig. 5.—Injection of direct inguinal hernia.

slightly so that its tip does not rest upon the bone and the injection started. At this point the needle point will lie either in or below the conjoined tendon. With the bladder empty, this region is a relatively safe one for injection because of the absence of important structures. The injection is completed as the needle is slowly withdrawn. Several injections are made in that region, the fluid being distributed along the area of insertion of the conjoined tendon. By slightly varying the injection angle (Fig. 5, *10, 11*) points medial and posterior to the pubic spine are infiltrated. It is important throughout this technique to make certain that one is in the safe area. If bone is not felt at the proper level, one should not inject, because it is possible to slip beneath the pubic ramus and endanger the bladder and peritoneum.

With properly performed technique, there is surprisingly little pain during this deep injection. The number of treatments given in the con-

joined tendon region vary from two to six depending upon the weakness of this structure as determined by preliminary examination. The induration following this treatment is often firmer than in the other portions of the canal, probably because of its relationship to the pubic bone. The last injections are made around the external ring itself. The crura are again infiltrated until it is certain that complete closure of the ring has taken place.

The perfect truss for hernial obliteration that can be worn comfortably day and night and in addition be waterproof has not been developed. Harris and White[39] have investigated this problem thoroughly and their paper describes the type of truss they recommend. Their important contribution rests on the recognition of the fact that the usual truss does not give properly directed pressure over the inguinal canal. This corresponds with our experience. It is necessary to modify the ordinary truss to make it suitable for injection therapy.

Harris and White advise the use of semirigid or rigid trusses with L-shaped extensions posteriorly pointing downwards toward the buttock. This revival of an old principle in truss construction changes the angle of pressure that the pad exerts. The fulcrum in the back of the truss directs the line of force through the inguinal canal at right angles to the truss pad. With the band of the truss properly placed midway between the crest of the ilium and the trochanter of the femur, it remains stationary and the pressure over the canal is at its maximum. We feel that the establishment of this principle is an important contribution to the problem of truss control.

Pads should be resilient and oval in shape. The truss is so adjusted that the lowest position of the pad is above the pubic crest. Thickening of the pad at one end is advisable. In indirect hernia it should be built up to exert more pressure over the internal ring. Conversely, in direct hernia, it should be thicker at the lower end.

A waterproof truss can be built on these principles. The frame may be of the semirigid type using phosphorbronze tubing. Rubber straps and pads can be added. Another arrangement is to have a leather-covered frame truss as a base and have the leather dipped in paraffin. The pads in this type may be of sponge rubber covered with paraffin-dipped leather. The usual precautions advised by previous writers must be carefully observed. In brief, the truss must be worn day and night until the completion of the treatment. We permit mild cases to sleep with an elastic truss but insist on the rigid appliance for daytime use. After completion of treatment, the patient is advised to continue the day truss for a period of three to six months, depending upon the severity of the case. Sleeping and bathing may be permitted without any truss soon after the last injection in many cases.

The technique just described is based upon cadaver studies in the Anatomy Department of the New York University Medical College. This technique has been used by us on over 200 patients in the past two years. These include clinic cases at the Stuyvesant Polyclinic and the private practice of one of us (H. I. B.). Approximately 3,500 injections, therefore, have been given by this method.

While a discussion of the permanency of cure is not within the scope of this paper, it has been noted that strict adherence to the method outlined above has given more definite results than previous haphazard procedures. Furthermore, as experience with this technique increased, intraperitoneal accidents became rare and the confidence of the operator increased. In the occasional cases of early recurrence, it was possible to determine the site of weakness and to reinforce this area by additional injections. Having a standard technique of this type makes the injection treatment more controllable and productive of better results.

A number of complications were noted in our series. Intraperitoneal injection with temporary shock occurred chiefly in the beginning of the study. The symptoms resulting from this type of insult generally subsided with rest in thirty minutes. In some cases of peritoneal shock the symptoms are due only to chemical irritation of the parietal peritoneum without actual penetration of this structure. This accident can be differentiated from peritoneal entry only by the comparative mildness of the symptoms and the absence of migratory pains. The only actual danger, in our opinion, with this treatment is the perforation of gut. Fortunately, this has never happened in our experience.

Hydrocele of the testicle or cord occurred rather infrequently (five times) in this study. Occasionally small nodules developed in the region of the external ring. These were either enlarged lymphatic glands or small cystic masses, difficult to diagnose. None of these fluid collections resulted in permanent pathology. The cord itself became temporarily swollen fairly often. Other edema noted were those of the subcutaneous tissues in the region of the inguinal canal, and muscle infiltrations at the internal ring in cases where fluid had diffused through these tissues. Mention should be made of transient puffiness over the pubic region and edema of the scrotum, sometimes with adhesion to the fascia of the cord or testicle. Sterility and impotence may be dismissed because of their complete absence in our experience which coincides with that of other writers, notably Rea.[35]

The efficiency of this technique in cases of postoperative recurrent inguinal hernia must be mentioned before concluding. However, the outstanding fact in our experience to date has been the ease with which children and young adults respond to this technique.

SUMMARY

1. The need for a safe technique in the injection treatment of hernia has been emphasized.

2. Modern injection treatment resembles the endofascial surgical approach.

3. The technique described herewith is based upon cadaver studies and a clinical experience of over 200 cases with 3,500 injections.

4. In indirect hernia the attack is centered upon the internal ring in the region of the transversalis fascia.

5. In direct hernia the injections are aimed at the region of the conjoined tendon. It is necessary to go outside of the inguinal canal in order to secure support for weakened structures.

6. This technique is based upon a series of safe angles which points the needle continually toward the pubic spine and its surrounding safe area. This minimizes the danger to important structures.

7. Truss control is as important as technique.

8. Increase in safety of injection coupled with standardization of technique places this procedure on a secure foundation.

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GYNECOMASTIA

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GYNECOMASTIA was first reported in the literature by Basedow[1] in 1848. His case was associated with hyperthyroidism, as were those reported by Starr,[2] Freeman,[3] Besley,[4] Menville,[5] and Sterling.[6] Starr's two cases improved after thyroidectomy, one of them returning to normal with the disappearance, also, of an accompanying narcolepsy. Dey[7] and Ramdas[8] each reported a case, and in these two no additional endocrine disturbances were noted, both young men having normal sex characteristics. These cases were treated by removal of the breasts. Tellgmann[9] reported a case following destruction of one testicle. Lewis and Geschickter[10] reported ninety-five cases from the Johns Hopkins Hospital pathologic records, some of which were associated with atrophy of the testicle and imperfect development of sex organs. These authors believe there is a definite relationship between the sex organs and gynecomastia, and state that 15 per cent of the cases begin at or shortly after puberty. They also state that malignancy has not been observed, but they quote Kriss,[11] Bailey,[12] Cairns,[13] Heidrich,[14] Ferguson,[15] and Hertzenberg[16] as emphasizing chorionepithelioma and teratoma of the testicle in relation to gynecomastia, and quote Roth[17] and Moehling[18] as reporting breast enlargement in men with hypophyseal tumors, and Mathias and Weber as describing gynecomastia in a man with a malignant tumor of the adrenal cortex. More recently Lisser[19] reported a case of adrenal cortical tumor in an adult male causing gynecomastia and lactation, and stated that a total of five cases had been reported in the literature, one of which, Holl's,[20] had survived operation, with a return to normal masculine characteristics. The others died. Lisser suggests that possibly a hormone which supports lactation, called cortilactin, is secreted in such large amount in adrenal cortical tumors as to cause the gynecomastia. Entwisle and Hepp[21] have had a case of testicular chorionepithelioma with pregnancy reactions, a positive Aschheim-Zondek, lactation, and pituitary changes like those in a pregnant woman. A case of unilateral gynecomastia in a 16-year-old colored boy is described by Cole and Elman.[22] This enlargement followed trauma to his chest. It was removed surgically. Edwards, Shimkin, and Shaver[23] observed the development of bilateral gynecomastia in the course of treatment of a case of Addison's disease with adrenal cortex extract. During a rest period in treatment, the breasts receded to almost normal, but increased in size when the treatments were resumed.

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At necropsy this patient's adrenal glands showed primary atrophy of the cortical glands and a marked preponderance of the chromophobe cells of the pituitary gland.

This evidence would seem to indicate a relationship between gynecomastia and any or all of the glands of internal secretion, but the testicle seems most constantly associated, whether there be atrophy, chorionepithelioma, or teratoma. From the standpoint of frequency, the thyroid, adrenal, and hypophysis seem to be associated in that order. In some of the cases there were found no discernible endocrine disturbances. The etiology, therefore, is still obscure. Moszkowicz said testicular secretion inhibits growth of the male breast. Kriss states that gynecomastia is not caused by cessation of inhibitory action of the testicles on the mammary glands.

The treatment, if any, has usually been surgical. The indication for surgical treatment, except in cases of definite tumors, has been embarrassment when dressed in a swimming suit, or fear of malignancy in the breast. There is seldom any real discomfort. It was because of embarrassment and fear of malignancy in the breast that the following cases presented themselves.

REPORT OF CASES

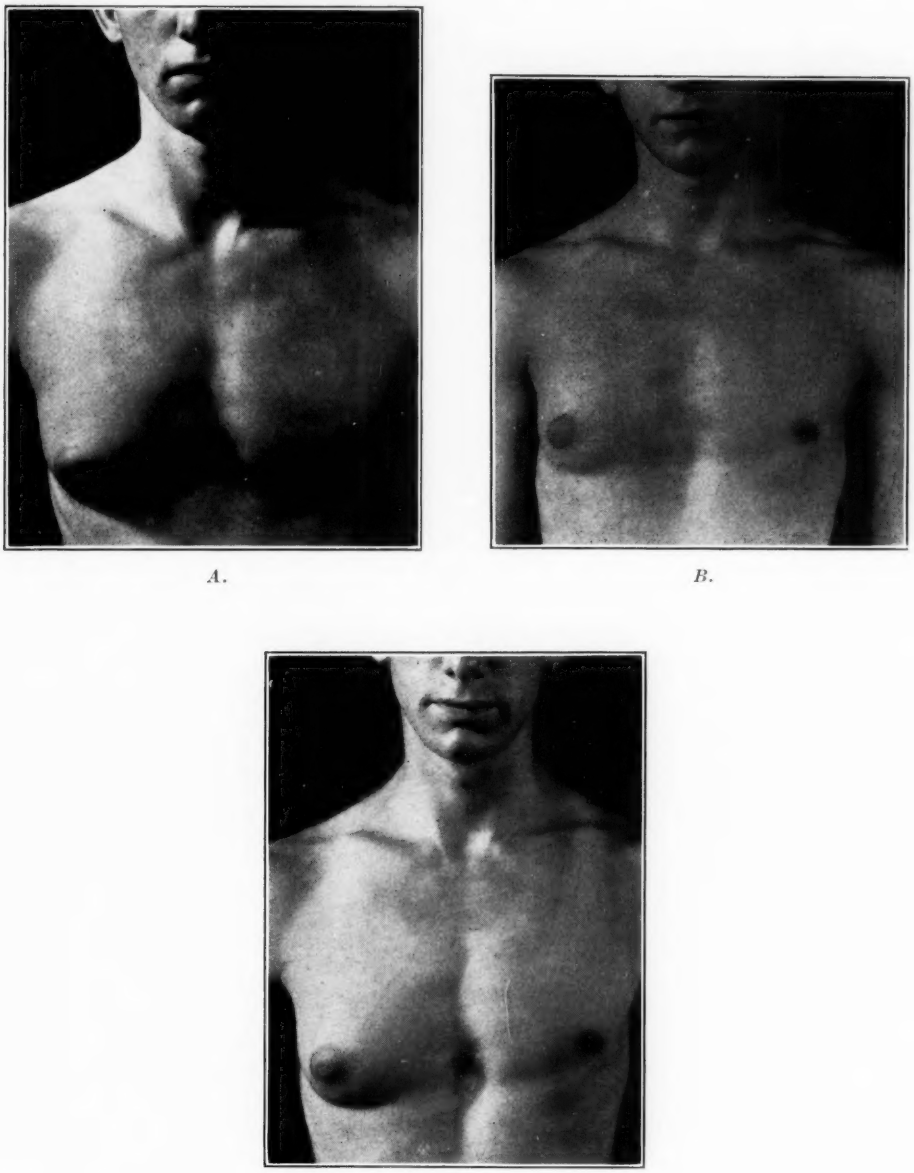
CASE 1.—P. E., Jr., aged 20 years, white male of small stature and slender build, was first seen June 22, 1936. He complained of a tender, enlarged breast on the right side which dated back three and one-half years to a blow over the right nipple by a baseball. The breast began to enlarge in four months and had been of the present size for two years (Fig. 1 *A*). In March, 1936, he had an appendectomy, and the breast decreased in size for twenty-four hours, only to return to its enlarged size suddenly within the next twenty-four hours.

Physical examination showed a well-developed right breast the size of that of an average 15-year-old girl. It was soft and of even consistency, there being no nodules. The areola was somewhat enlarged. The left side was normal. The right testicle was normal, but the left one was about half as large as the right. The voice was masculine. Hair was sparse on the face, requiring a shave once in a week or ten days. Hair was somewhat sparse also in the axillae and at the pubis. The penis was rather small. The Aschheim-Zondek test on his urine was negative. There were no other findings of significance.

Before resorting to surgical removal of the breast, it was decided to try hormone therapy, on the theory that, if the small left testicle could be made to enlarge to normal size, the breast might recede. Beginning July 20, 1936, he was given, twice a week, an injection of anterior pituitary-like hormone, there being given a total of 10 c.c. in five divided doses. By Aug. 3, 1936, there was no noticeable change in breast or testicle, and on Sept. 28, 1936, treatment with male sex hormone, testosterone propionate,* was begun intramuscularly. The first twenty-one doses, given twice a week, were each 2.5 mg. per dose. By Oct. 29, 1936, there was an appreciable decrease in the size of the breast and increase in the size of the left testicle. The fourteenth dose was given on Dec. 21, 1936, and at this time the left testicle was half again the size it was when testosterone treatment was instituted, but the breast had shown no further change. The patient said he had to shave oftener. On Jan.

*The testosterone propionate used in these cases was oreton, which was kindly furnished by the Schering Corporation, Bloomfield, N. J.

25, 1937, the penis seemed larger, the breast was about one-half its original size, the left testicle seemed a little larger, and the patient was shaving three times a week. On March 15, 1937, the dosage of testosterone was increased to 5.0 mg., this being the twenty-second dose. At this time the left testicle was almost equal to the right in size, and there was little more, if any, change in the breast. After seven 5.0



A. *B.*

C.

Fig. 1.—*A*, Case 1, showing enlarged right breast in June, 1936, before treatment. *B*, Case 1 in June, 1937, after having received 87.5 mg. of testosterone propionate in twenty-eight divided doses. Treatment was continued with 25.0 mg. doses until a total of 462.5 mg. had been given without further change. The breast has decreased markedly in size, but it is still larger than the unaffected side. *C*, Case 1 in July, 1938, showing recurrence of one month's standing. He had received no treatment for ten months but, since the photograph was taken, injections have been resumed. However, over a period of three weeks, 165.0 mg. of testosterone propionate have been given without effect.

mg. doses had failed to produce further improvement, the dose was increased to 25.0 mg. each on June 28, 1937. A photograph was taken at this stage (Fig. 1 *B*) which was just a year from the time the patient was first seen, and after he was given a total of twenty-eight injections. At this time the left testicle had increased to almost the size of the right, and the breast had decreased to less than one-third its size when first seen. The hair on his face had become heavier, and he was shaving every other day. Libido was increased. Treatment with 25.0 mg. doses was continued irregularly until Sept. 23, 1937, without apparently any further change, and discontinued with the forty-third dose on that date. The patient felt no more embarrassment, was more decidedly masculine in character, and was pleased with the result.

On July 11, 1938, the patient returned to the clinic. His right breast was fully as large as it was when he first was seen on June 22, 1936. His left testicle was apparently as small as it was at that time and measured 1 3/16 by 3/4 by 15/16 inches. The right testicle measured 1 9/16 by 1 3/16 by 1 inches. A photograph (Fig. 1 *C*) of

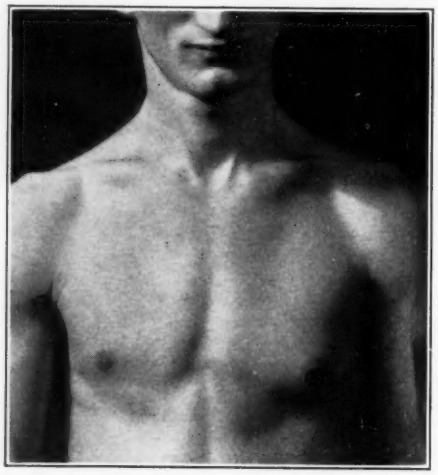


Fig. 2.—Case 2, in whom there was no change after prolonged treatment with large doses of testosterone propionate. He has also received anterior pituitary substance without effect. This patient is five years older than the patient in Case 1.

the breast at this time shows it to be almost identical in appearance with that of the first photograph (Fig. 1 A), taken before treatment was started in June, 1936. This recurrence was noticed only five weeks before the patient reported on July 11, 1938, and developed rapidly to its present size without history of trauma. Treatment with testosterone propionate was started with 10.0 mg. doses three times a week, and, after the fourth dose, it was increased to 25.0 mg. three times a week. By Aug. 1, 1938, he had had 165.0 mg. in three weeks without any apparent change in the breast. The atrophied testicle, however, had enlarged slightly, measuring 1 5/16 by 5/8 by 1 inches. Libido was increasing rapidly, and hair on the face was again growing faster. Testosterone propionate, 25.0 mg. per dose, is being continued three times a week.

CASE 2.—J. A., Jr., aged 24 years, a white male of average height, but slender, first seen at the clinic on July 25, 1936, complained of an enlargement of his left breast. Five years previously he was struck over his left chest with a bundle of books. The left breast became enlarged and remained the same size to date. He sought advice because of fear of malignancy, rather than from embarrassment. He is married and the father of two children.

Physical examination revealed a somewhat enlarged breast on the left side (Fig. 2) which was slightly tender on palpation, but not painful. The nipple was not much larger than the right. There were no hard nodules present, but some glandular tissue was palpable. This breast was not as large as that in the previous case. The testicles were equal in size. The Aschheim-Zondek test was negative. The thyroid was palpable, and the basal metabolic rate was plus 16. There were no signs of hyperthyroidism, and physical findings were otherwise negative.

Treatment with testosterone propionate was started on Nov. 8, 1936. Injections were given twice a week. There were rest periods from one to three weeks scattered throughout the course. The first twelve doses were 2.5 mg. each, the next ten were 5.0 mg. each, and from the twenty-third through the fifty-first the dose of each injection was 25.0 mg. The last injection was given on Sept. 1, 1937, when treatment was discontinued because there was no appreciable change in the size of the breast. This patient had received eight more injections, and more concentrated dosage, than the preceding one, without a favorable result. During June and July, 1938, this patient received anterior pituitary substance intramuscularly two or three times a week without effect. The breast is unchanged.

CASE 3.—M., aged 24 years, a single white male of average height and quite well built, was seen once only, on March 5, 1938. He had a right breast similar to that described in Case 1. At the age of 16 years he received a blow on the right chest while boxing. The breast immediately became swollen and tender, and gradually increased in size during the next two years, since which time it has been unchanged. Libido was normal.

Examination revealed a well-developed right breast, with a slightly enlarged nipple and areola. There were a few small firm nodules present, and they were quite tender on palpation. The glandular structure was easily felt. There was no secretion. The left testicle, which the patient thought was the larger, was in fact smaller than the right. There was a moderate varicocele on the left side. He was otherwise normal and decidedly masculine.

Photographs, laboratory work, and treatment were not possible in this case, as the patient did not return. Certain points are of interest for comparison with the two previous cases and will be discussed later.

CASE 4.—E. McC., aged 16 years, colored, well developed for his age, came to the clinic on April 18, 1938, because of double breast enlargement which had been present two years. He associated this enlargement with a fall across the handlebars of his bicycle, wherein both sides of his chest were injured. He gave a history of having had an undescended testicle on the left side. At the age of 9 years, when seen in the dispensary, the left testicle was still undescended. The testicle is now in the scrotum, but the patient is not sure about the time of its descent. Two years ago he was operated upon for a right inguinal hernia. He is in the eighth grade in school and ascribes his apparently slow progress to having been out of school at different times, claiming that he has no difficulty in keeping up with the other students in his classes. When first seen, the patient gave a history of not having had an erection or any other signs of libido.

Physical examination revealed a strong looking boy in good physical condition. He seemed to be of average intelligence. Both breasts were enlarged and dome-shaped, with the left being slightly larger than the right. The nipples and areolae were swollen and enlarged to twice the normal size. Glandular tissue was palpable in the breasts, but there were no hard nodules. They were very slightly tender on palpation. Both testicles were in the scrotum, but the left was about two-thirds as large as the right. The penis was normal in size. The Aschheim-Zondek test of his urine was negative. His basal metabolic rate was minus twelve. There were no other findings of note.

Treatment with testosterone propionate was started on May 11, 1938. The initial dose was 25.0 mg. and was given intramuscularly. The treatments were given approximately three times a week. On May 22, 1938, when he received his sixth injection, his breasts were definitely smaller. On June 6, 1938, when he received his tenth injection, both breasts showed a marked decrease in size. At this time the atrophied left testicle was almost as large as the right, there was more pubic hair,

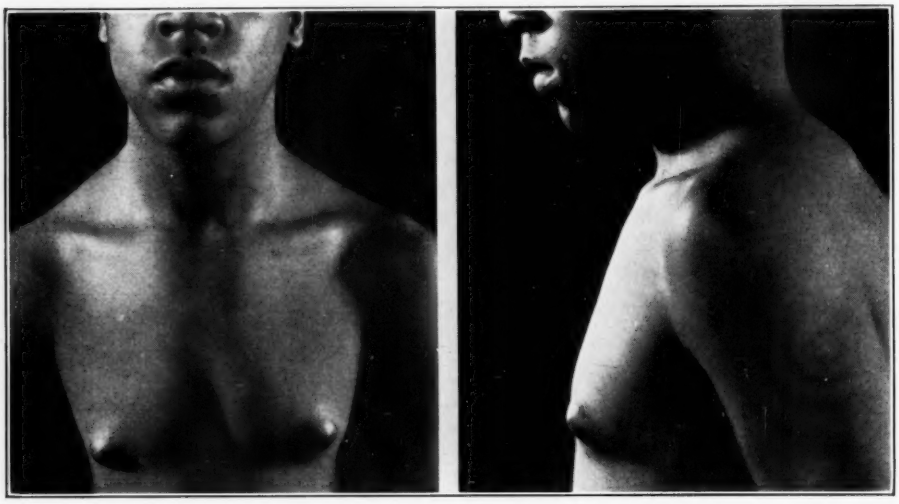


Fig. 3.—Front, *A*, and side views, *B*, of Case 4, who is 16 years of age, before treatment.

Fig. 4.—Front, *A*, and side views, *B*, of Case 4 after having received a total of 320 mg. of testosterone propionate in the course of two months. A definite reduction in size of the breasts will be noted.

and he seemed to act a little livelier. Libido was still absent. On June 13, 1938, his breasts were practically flat, the nipples were normal in appearance, and his testicles were very nearly equal in size. At this time he had received a total of 300 mg. of testosterone propionate, in twelve doses. Because the breasts and testicle seemed to have been brought back to normal, the dose of each injection was reduced to 10.0 mg. and continued three times a week to determine what effect, if any, these additional

treatments might have on libido. On June 27, 1938, the patient stated he had had his first erection a few days previously. By July 18, 1938, he had received a total of 405.0 mg. of testosterone propionate in a little over two months. Libido had been decidedly increased, the penis was much larger, and calibration of his testicles showed the right to measure 1⅝ by 1 by 15/16 inches and the left 1 3/16 by 15/16 by ⅞ inches. On Aug. 1, 1938, the left testicle measured 1½ by 1⅛ by ⅞ inches, and the penis was still larger than at the time of the examination a week previous. Treatments are to be continued if necessary once a month or oftener to maintain the present favorable result. Figs. 3 *A* and *B* show front and side views of this patient before any treatment was given. Figs. 4 *A* and *B* show corresponding views after 320 mg. of testosterone propionate had been given in fourteen doses.

COMMENT

Four cases of gynecomastia herein reported have certain similar characteristics. All but Case 4 were unilateral. All gave a history of trauma. All occurred while the patients were in their "teens." No one of them showed any evidence of disturbance in any of the glands of internal secretion except the testicles, and all but Case 2 had an atrophied left testicle. The Aschheim-Zondek test was negative in the three that were given treatment. The other (Case 3) was not examined, for reasons previously given. Libido was increased in two of the three treated cases and was very much present in Case 3, who was not treated.

These cases are among the first observed with testosterone therapy. Bronstein[24] reported a case of the less frequent bilateral type treated with androsterone and testosterone propionate. His patient was a 17-year-old colored boy with atrophied testicles, a positive Friedman test, no libido, no secretion from the breasts, and a rather effeminate personality. After treatment with androsterone, and later testosterone propionate, he noted the following suggestive changes: (1) Appearance of erections, and hair on the face, chest, and legs; (2) noticeable interest in the opposite sex; (3) questionable enlargement of testes and shrinkage of right breast.

A case of unilateral (left-sided) gynecomastia in a boy 14 years of age is now being treated with testosterone propionate by Birnberg, Kurzrok, and Livingston.[25] They report "the breast has become considerably smaller, but the patient is still under treatment." They are giving 10.0 mg. of testosterone propionate twice a week.

Wolf[26] advises that injection of androtin and anterior pituitary-like substance generally results in a decrease in the size of the breast. He recommends pituitary and adrenocortical hormone substance to stimulate testicular development if there is merely hypofunction of the testicles. If Case 2 were merely one of testicular hypofunction, for the testicles were equal in size, it might have been expected that testosterone would stimulate them enough to cause at least some change in the breast, but it had no apparent effect. Nor has anterior pituitary substance had any effect in this patient after two months' treatment.

The favorable results obtained in Cases 1 and 4, as opposed to the unfavorable result in Case 2, in spite of the fact that they all received practically the same treatment, may be due to two factors. In Cases 1 and 4, which responded to treatment, there was marked atrophy of the left testicle, while in Case 2 the testicles were equal in size and apparently normal. In Cases 1 and 4 the breast enlargement occurred earlier after puberty (at 16 and 14 years respectively) than Case 2 who was 19 years of age when his breast enlarged. Cases 1 and 4 were also considerably younger than Case 2 when endocrine therapy was given. Case 4, whose breasts enlarged at 14 and whose treatment was given at 16, responded more quickly than Case 1, whose breast enlarged at 16 and received treatment at 20. Age, therefore, may be an important factor. In view of our meager experience a good prognosis with hormone therapy would appear to be dependent upon the development of gynecomastia soon after puberty, and likewise upon the institution of treatment at an early age. Testicular atrophy seems to be definitely associated in a large percentage of cases, particularly so far as the efficiency of testosterone therapy is concerned.

The favorable outcome in two out of three cases of gynecomastia treated with testosterone propionate suggests that in cases of this kind endocrine therapy should be given a thorough trial before surgical removal of the breast is advised. The spontaneous recurrence of the right breast in Case 1, associated with recurring atrophy of the left testicle, suggests that probably replacement therapy with male sex hormone at regular intervals will be found necessary to maintain a cure once it has been effected.

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THE REMOVAL OF BENIGN TUMORS OF THE BREAST WITHOUT VISIBLE SCARS

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TO THE person of aesthetic sense, a disfiguring scar engenders an inferiority complex, continuously activated by the physical deformity. To a sensitive woman scars upon exposed portions of the body and breasts are especially objectionable. In the past incisions radiating from the nipple which leave such scars have commonly been employed for the drainage of abscesses and the excision of benign tumors. But the skin overlying the mammary gland is very elastic and, aided by the underlying loose fascia, nearly any portion of the gland may be brought near the margin of the areola for excision. Aseptic incisions along the areolar margin, accurately closed, heal with an imperceptible scar, in marked contrast with the ugly disfigurement seen after incisions elsewhere. The common blue dome cysts of the breast forming well-rounded, tense masses from the size of a pea to that of a large marble may give the sensation of a solid tumor, but as a rule they are more perfect spheres or ovals. They may readily be aspirated through a rather fine hypodermic needle, and the remaining sac is so thin that no perceptible thickening remains. As these cysts, which may be multiple, seem to have no malignant tendencies, we have for years treated them by aspiration. Apparently none of those aspirated have refilled. Of course, if the needle indicates that a solid tumor has been entered, or if residual thickening remains, then exploration and biopsy are indicated.

For the removal of benign tumors, a curved incision along that part of the areolar border nearest the tumor is made. The fascia close to the gland is incised and opened by introducing and separating the blades of a Mayo scissors. Using long narrow retractors, the tissue separation or division is continued until the tumor is reached and grasped with a tenaculum or viscera forceps, and, aided by retraction, pulled into view. By dull or sharp dissection the tumor is enucleated, bleeding points being at once ligated before the tissues have retracted from view. Obliteration of the cavity left after removal of the tumor by the use of sutures is rarely necessary or desirable and may cause distortion of the breast. Even multiple tumors, lying along the periphery of the mammary gland, may be removed through the areolar incision.

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If the tumor is too large to be delivered through the stretched areolar incision, it may be removed by morcellation or through an incision along the thoracomammary sulcus, where the scar will be

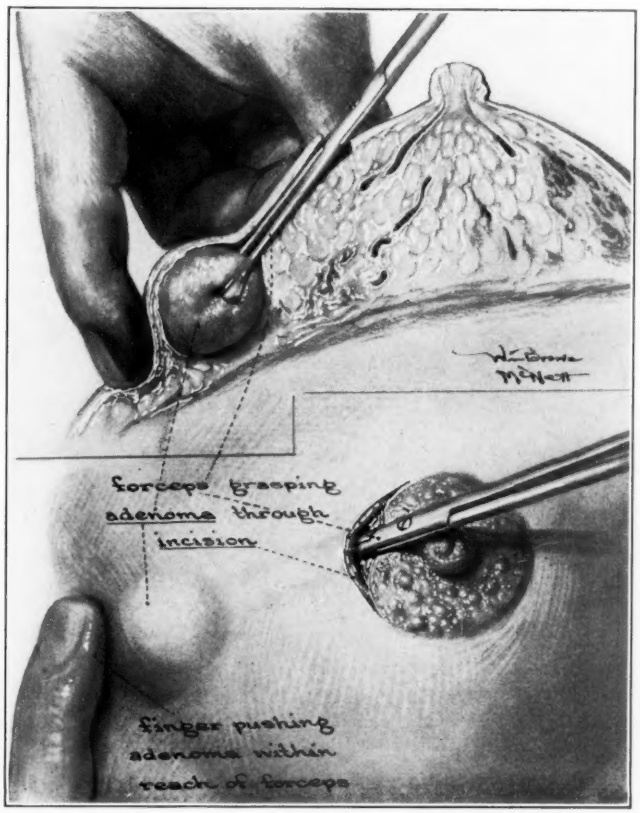

Fig. 1.—The removal of benign tumors of the breast without visible scar. A crescentic incision is made along the areolar border on the side toward the tumor. The deep fascia is tunneled by blunt dissection to the site of the tumor. Aided by narrow retractors and palpation, the tumor is grasped by forceps, brought into view, and enucleated. Each bleeding point is ligated before the retracted tissues are released. Finally, the areolar wound is closed with fine interrupted dermal sutures.

hidden by the overhanging breast. The latter incision is, of course, the best approach to all deep abscesses of the gland. Fine silk which causes less tissue reaction than catgut is preferred for ligatures in the aseptic wound, and very fine (36 gauge) alloy steel wire for the interrupted sutures to approximate the skin margins.

NONFATAL RUPTURE OF THE LEFT MAIN BRONCHUS FROM EXTERNAL TRAUMA

Report of Case

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THE infrequency of rupture of a bronchus from external trauma and the rarity of recovery from an injury of this type prompt our presentation of the following case.

CASE REPORT

A white woman, 22 years of age, was admitted to Memorial Hospital the afternoon of Jan. 1, 1938, a few minutes after she had been involved in an automobile accident. She had been unconscious for a few moments immediately after the accident. On regaining consciousness, moderate dyspnea and substernal pain were noted. Dyspnea increased and at the time of admission to hospital she was orthopneic, but rational, apprehensive, and complaining of difficulty in inspiration. There was a small laceration over the left eye and moderate subcutaneous emphysema of the neck, face, the wall of the thorax, and over the shoulders. The pulse rate was 118 and of fair volume. Respirations were 32, shallow, and labored. The systolic blood pressure was 120 and the diastolic 80.

Physical examination of the thorax revealed bilateral limitation of respiratory excursion with a tympanitic percussion note over both sides anteriorly. The breath sounds and percussion note were altered by subcutaneous emphysema, but the mediastinum was thought to be displaced toward the left side. Contusions were present over the sternum. A diagnosis was made of rupture of both lungs with bilateral tension pneumothorax.

The subcutaneous emphysema increased rapidly and within five minutes after the patient was seen, the shoulders, neck, and face were three or four times their normal size. Air was felt in the tissues over the lower abdomen, over the shoulders and arms to the wrists, and almost to the hair line of the scalp. Dyspnea became much more pronounced and it seemed that respiration would soon cease. The systolic blood pressure dropped to 60, the pulse became thready with a rate over 180, and marked cyanosis was noted. The patient became unconscious and appeared to be in extremis.

A short incision was made in the suprasternal notch, and the tissue was dissected behind the upper manubrium. Large quantities of air escaped from the wound. A small needle cannula was inserted into the intercostal space on the left side outside the nipple line, and about 700 c.c. of air were withdrawn from the thorax by reversing elevation of the bottles of the pneumothorax apparatus. The initial pressure on the left side was plus 2 c.c. of water; the final pressure, minus 4. The same procedure was employed on the right side with the aspiration of 7,000 c.c. of air; the initial pressure was plus 4 and the final pressure minus 3.

Following aspiration of air from both sides of the thorax and the employment of artificial respiration, the patient began to breathe, regained consciousness, and

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cyanosis almost disappeared. The pulse rate dropped to 130, and the systolic blood pressure rose to 105. The mediastinum shifted to its normal position. The patient was placed in an oxygen tent, and 12 liters of oxygen per minute were administered.

Thirty minutes later she suddenly became quite dyspneic, lapsed into unconsciousness, became extremely cyanotic, and the pulse was almost imperceptible. Shallow respirations occurred about three or four times per minute. A silver cannula, such as that devised by Bigger,[1] was placed through the third right intercostal space into the pleural cavity, and several liters of air escaped under pressure. The cannula was strapped in place and covered with a rubber dam, allowing the egress but not the ingress of air. Respirations increased to 50 or 60 per minute. The pulse became palpable, and consciousness was regained. A transfusion of 500 c.c. of whole blood was given. At this time roentgenoscopic examination of the thorax, using a portable apparatus, showed bilateral pneumothorax, more marked on the left side.

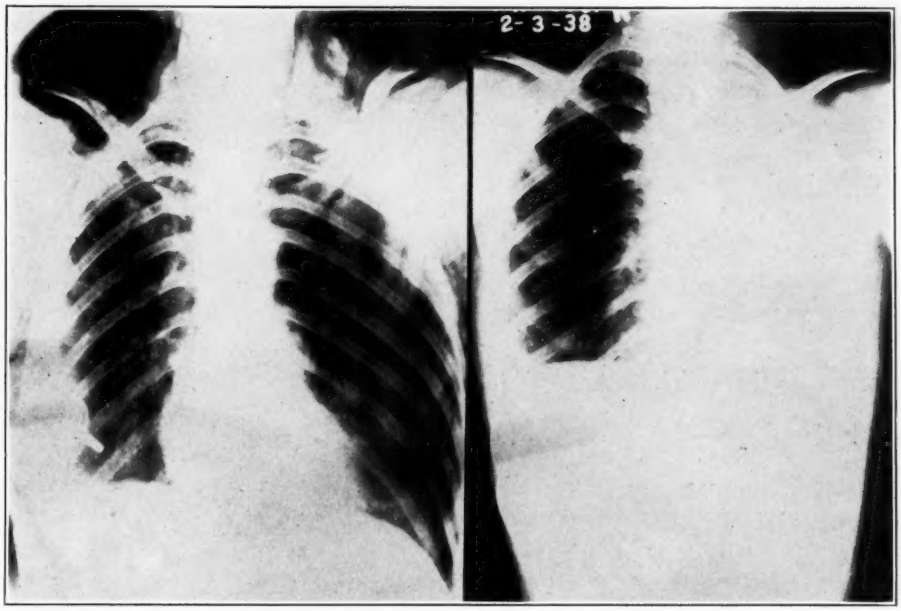

Fig. 1. Fig. 2.

Fig. 1.—Roentgenogram showing bilateral pneumothorax and emphysema of the tissues of the neck; silver cannula is in place on the right side.

Fig. 2.—Roentgenogram showing complete atelectasis of the left lung at the time of dismissal.

Because of the relatively rapid respiration, repetition of the aspiration of the left thorax was deemed advisable and, accordingly, 950 c.c. of air were withdrawn. The initial pressure was plus 1, and the final pressure minus 11. About three hours later 300 c.c. of air were again removed from the left thorax. At 1:30 on the morning of Jan. 2 it was necessary to transfer the cannula on the right side to the region of the axilla because of emphysema and edema at its previous location. Fourteen hundred c.c. of air were again aspirated from the left side of the thorax.

The patient's condition gradually improved until the morning of Jan. 4, when the mediastinum suddenly shifted to the left side and the respiratory distress increased markedly. On physical examination complete atelectasis of the left lung seemed to be present. Bronchoscopy was considered, but it was thought best to treat the patient expectantly. Cough was encouraged, and expectoration of a consider-

able amount of mucopurulent secretion was followed by gradual improvement. The intercostal cannula was removed from the right side on Jan. 5, and from that time the patient's improvement progressed rapidly. The ribs seemed to be intact, but a film taken Jan. 12 showed transverse fracture of the first rib on the right side, located 1 inch from the costochondral junction.

The patient was discharged from hospital Jan. 14, at which time the left lung was totally atelectatic. The right lung was apparently normal. Re-examination on Feb. 3 showed that the atelectasis of the left lung had not changed. During the interval between dismissal and re-examination she had been in relatively good condition except for slight dyspnea on exertion and a moderate cough productive of mucoid secretion. Bronchoscopic examination was recommended to determine the cause of the atelectasis.

Bronchoscopy revealed a longitudinal area of necrosis on the posterior wall of the left main bronchus, beginning at the junction of the bronchus and trachea and extending 1½ inches to a healing bronchial stricture. The lumen of the stricture was about 2 mm. in diameter. No secretion was present. It was deemed inadvisable to attempt to introduce dilating forceps into the stricture because of the acuteness of the reaction surrounding the lesion. The condition observed at bronchoscopy was considered representative of partial rupture of the bronchus with healing and formation of stricture.

The patient has been observed at monthly intervals and when last seen, five months after the accident, she was quite well and able to carry on her duties as a secretary.

COMMENT

In 1912, Schönberg[7] collected fifteen cases of fatal rupture of a bronchus in which compression of the thorax was the etiologic factor. In four of these cases no evidence of skeletal fracture was apparent. King,[2] Mumford,[5] and Thomas[8] each reported similar cases without skeletal fracture. In 1928, Krinitzki[3] reported the only case of recovery from this type of lesion. Rupture of a bronchus was not recognized at the time of the accident, but was discovered at post-mortem examination twenty-three years later. Meade and Graham[4] in 1930 summarized the previously reported cases and added one of their own, which was diagnosed at post-mortem examination, death having occurred sixteen hours after the accident. In discussing thoracic readjustment following total and partial pneumonectomy, Rienhoff[6] reported two patients with post-traumatic atrophy of the left lung, who were operated on for release of extrapericardial adhesions. The initial injury was not described. In both instances a crushing injury of the thorax in early childhood was apparently the etiologic factor.

From a review of the literature it would seem that the case we are reporting is unique in that the patient has recovered from the accident and the lesion has been identified during life. It is possible, of course, that infection may occur in the lung distal to the stricture, but to attempt bronchoscopic dilatation of the stricture does not seem wise at this time. If infection should occur, pneumonectomy may be indicated.

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ACETYLATION OF SULFANILAMIDE

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THE conjugation of certain benzene ring compounds containing the amine radical has been observed repeatedly in various species.[1] The acetylation of another such compound, para-amino-benzene sulfonamide, or sulfanilamide, has been demonstrated by Marshall and his co-workers[2] in certain species, including man and the rabbit. The acetylated form of the drug becomes widely distributed in the body tissues and appears in the blood and urine. The site of the process of acetylation has been a matter of speculation, although the recent in vitro experiments of Harris and Klein[3] implicate the liver. The present report concerns itself with a study of the acetylation of this drug in the rabbit.

PLAN OF EXPERIMENT

In order to determine the site of acetylation, surgical extirpation of one or more of the organs in question was performed, after which sulfanilamide was given by vein. The concentrations of free and acetylated sulfanilamide in the blood were determined at intervals subsequently. Rabbits weighing 1.5 to 2.5 kg. were used. They were divided into four groups, each group containing at least four animals. Group 1 constituted normal controls. The second group consisted of bilaterally nephrectomized animals. In the third group the gastrointestinal tract from gastric cardia to the rectum was excised, along with the pancreas and the spleen. In Group 4 total hepatectomy was performed, after first removing the gastrointestinal tract, the spleen, and the pancreas. In this group also there was one animal in which only subtotal hepatectomy was done.

The operations were all performed in one stage under ether anesthesia with a minimum of trauma. The animals were given 10 to 20 c.c. of 2.5 per cent glucose in 0.9 per cent sodium chloride solution by vein immediately after the operations. Precautions were taken against loss of body heat during and after operation. Standard doses of 0.75 gm. of sulfanilamide, dissolved in 20 to 30 c.c. of warmed water or 0.9 per cent sodium chloride solution, were given intravenously from one to three hours after operation. Blood samples were taken from the

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marginal vein of the ear or by cardiac puncture at stated intervals. Concentrations of both free and acetylated sulfanilamide were determined on oxalated whole blood by the method of Marshall and others.[2]

PRESENTATION OF DATA

In Chart 1 are shown graphically the concentrations in the blood of free, acetylated, and total sulfanilamide following an intravenous injection of 0.75 gm. sulfanilamide in the normal rabbit under ether

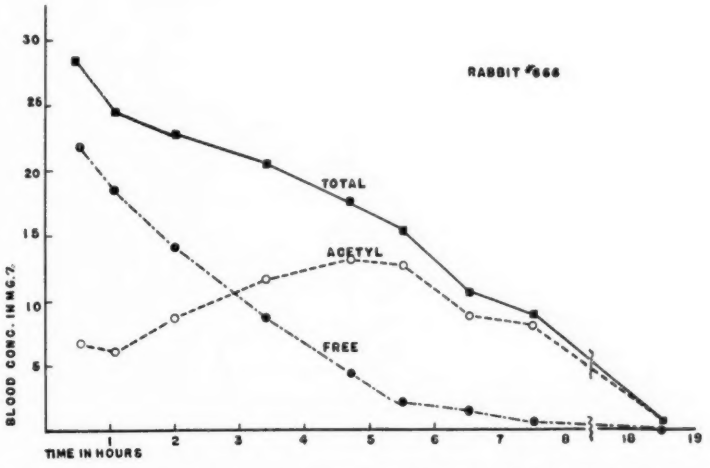

Chart 1.—Blood concentrations of total, free, and acetylated sulfanilamide in the normal rabbit after intravenous injection of 0.75 gm. sulfanilamide.

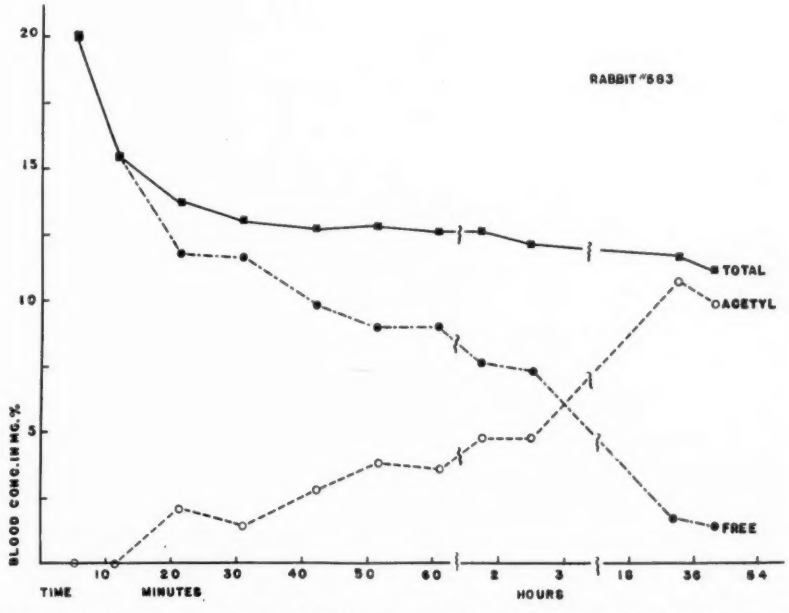

Chart 2.—Blood concentrations of total, free, and acetylated sulfanilamide after intravenous injection of 0.75 gm. sulfanilamide in the bilaterally nephrectomized rabbit.

anesthesia. The results are to be compared with data obtained in similar manner from a bilaterally nephrectomized rabbit, as shown in Chart 2. The data shown in Charts 1 and 2 are typical of the findings in the two groups. In Table I are presented data obtained in a study of six rabbits after removal of the gastrointestinal tract, spleen, and pancreas. Table II shows the results obtained in six experiments, includ-

TABLE I

BLOOD CONCENTRATIONS OF SULFANILAMIDE AFTER INTRAVENOUS INJECTION OF FREE SULFANILAMIDE IN RABBITS SUBJECTED TO GASTROENTERECTOMY, SPLENECTOMY, AND PANCREATECTOMY

RABBIT NUMBER	FREE SULFANILAMIDE mg. %	ACETYLATED SULFANILAMIDE mg. %	TOTAL SULFANILAMIDE mg. %	PERCENTAGE ACETYLATED %	TIME AFTER ADMINISTRATION hr.
571	3.7	19.5	23.2	84.2	3.5
	2.1	15.2	17.2	87.8	6.0
570	8.3	2.7	11.1	24.3	2.5
	10.6	7.9	18.5	42.7	8.0
572	8.5	4.0	12.5	32.0	2.0
	8.7	4.6	13.3	34.5	3.0
573	9.3	2.5	11.8	21.3	1.9
	9.8	3.8	13.6	27.8	2.9
574	10.1	2.2	12.3	17.8	2.5
575	9.3	4.5	13.8	32.6	2.5

ing one in which 94 per cent of the liver tissue was removed without fatal impairment of the portal circulation. In the other five experiments total hepatectomy with removal of the gastrointestinal tract, spleen, and pancreas was performed.

DISCUSSION

These experiments are open to the criticism to which all extirpation studies are liable; namely, the removal of an organ may disturb interlocking mechanisms and produce effects in the functioning of related viscera which confuse the picture. To this consideration must be added the uncertain effects of recent trauma, even though minimized by gentle surgical technique, careful hemostasis, and avoidance of heat loss. The acetylating process, however, seems to be carried on as a fundamental part of cell behavior, as attested by the uniformity of our results under varying conditions, and as seen in the in vitro experiments of Harris and Klein on liver slices.

When sulfanilamide is given intravenously in the normal rabbit, acetylation takes place with striking rapidity. As seen in Chart 1, 25 per cent of the total blood sulfanilamide is in the acetylated form, even as early as one-half hour after the injection. Chart 1 also illustrates the fact that the proportion of acetylated sulfanilamide in the blood rapidly increases, while the free sulfanilamide decreases. In the nephrectomized rabbit, as shown in Chart 2, where the concentration remains

TABLE II

BLOOD CONCENTRATIONS AFTER INTRAVENOUS INJECTION OF SULFANILAMIDE (RABBITS 101, 574, 523, 557, 589, 591 PREVIOUSLY SUBJECTED TO REMOVAL OF LIVER, GASTROINTESTINAL TRACT, SPLEEN, AND PANCREAS; RABBIT 465 PREVIOUSLY SUBJECTED TO SUBTOTAL HEPATECTOMY)

RABBIT NUMBER	PERCENTAGE OF LIVER REMOVED	FREE SULFANILAMIDE	ACETYLATED SULFANILAMIDE	TOTAL SULFANILAMIDE	PERCENTAGE ACETYLATED	TIME AFTER ADMINISTRATION
	%	mg. %	mg. %	mg. %	%	hr.
465	94	13.4	0	13.4	0	2.2
		13.5	0	13.5	0	3.9
		13.3	1.2	14.5	8.3	4.5
		13.0	1.1	14.1	7.8	5.5
101	100	9.0	0	9.0	0	3.0
574	100	6.4	0	6.4	0	2.0
		5.9	0	5.9	0	3.0
523	100	17.0	0	17.0	0	2.2
		16.8	0	16.8	0	4.0
		16.9	0	16.9	0	5.5
		15.5	0	15.5	0	6.2
557	100	4.0	0	4.0	0	2.0
		3.9	0	3.9	0	3.7
		4.2	0	4.2	0	4.8
		3.9	0	3.9	0	5.8
589	100	20.0	0	20.0	0	2.5
		18.0	0	18.0	0	3.6
		16.0	0	16.0	0	5.3
591	100	14.0	0	14.0	0	1.5
		14.0	0	14.0	0	2.7
		13.0	0	13.0	0	4.5
		11.5	0	11.5	0	5.4
		11.0	0	11.0	0	6.2

steady through absence of excretion, all the blood sulfanilamide soon becomes acetylated. Acetylation, then, seems to be a unidirectional process, dependent upon time rather than concentration of free sulfanilamide in the blood. This is perhaps an important consideration in the clinical use of the drug, for there is some reason to believe that acetylated sulfanilamide is less bacteriostatic than is the free form.[4]

Concerning the locus of acetylation, the evidence from these experiments is clear. In Table I it is seen that acetylation proceeds rapidly in the rabbit deprived of gastrointestinal tract, spleen, and pancreas, and in one such preparation, Experiment 571, the process is 84 per cent complete at the end of 3.5 hours. As pointed out above, acetylation occurs at a normal rate in the nephrectomized animal. Attention is thus focused on the liver. In the rabbit it is impossible to remove all the liver in one operation without the rapid onset of prostration and death from portal stasis. However, it is possible to remove all but the small caudate lobe closely adherent to the portal vein, comprising about 10 per cent of the liver substance, and have the animal survive from

12 to 24 hours. In such preparations, as shown in Table II, acetylation occurs, but at a greatly reduced rate. In Experiment 465, in which the animal was deprived of 94 per cent of the liver, the blood at the end of 5.5 hours contained about 8 per cent of the total sulfanilamide in the acetylated form. Other experiments, not described here, show that after 80 to 90 per cent of the liver tissue is ablated the rate of acetylation falls off sharply. On considering the responses of the totally hepatectomized rabbits, subjected also to gastroenterectomy, splenectomy, and pancreatectomy, we find that these animals in no case show power to acetylate, even though the survival period is 18 to 24 hours. Thus it seems clear that acetylation of sulfanilamide does not occur in the absence of the liver.

In Chart 2, which shows data typical of the findings in nephrectomized animals, one sees confirmation of the conclusion of Marshall and others[2] and of Stewart, Rourke, and Allen[5] that sulfanilamide is excreted only through the kidneys. The ready diffusibility of the drug also is demonstrated, for within 30 minutes after the intravenous injection was made a steady total sulfanilamide concentration has been reached. The stability of this level suggests that the acetylated molecule is also highly diffusible, and that it likewise enters the body fluid mass freely.

CONCLUSIONS

1. The liver is the site of acetylation of sulfanilamide in the rabbit.
2. In subtotal hepatectomy the rate of acetylation is reduced.
3. Following the intravenous injection of sulfanilamide in the bilaterally nephrectomized rabbit, a steady concentration of total sulfanilamide in the blood soon results, but acetylation progresses until the free form is present in only minimal concentrations.

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THE ORGANIZATION AND TECHNIQUE OF THE BLOOD BANK AT THE PHILADELPHIA GENERAL HOSPITAL

Experiences With 1,000 Transfusions

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INTRODUCTION

EARLY in 1937 the administrative staff at the Philadelphia General Hospital decided to investigate and standardize the procedure of blood transfusion. For this purpose, a committee of the surgical staff was appointed to work with the chief surgical resident. The use of conserved, defibrinated cadaver blood had been considered and given a brief trial, but it was decided to adopt the citrate method of transfusion as the standard method of the hospital, since this offered a technical simplicity over the somewhat exacting and more elaborate direct methods. Moreover, there were no clinical disadvantages apparent in a large experience with its use.

Regardless of the method of transfusion, the selection of a donor had previously been a time-consuming and labor-wasting effort. The reasons for this are as follows: (1) For every patient needing a transfusion, a number of donors must be called to the hospital to be typed, in the hope that one of them will be in the desired blood group. (2) Serodiagnostic tests must be done on the blood of every donor, requiring a trained technician to be on call at all times, unless, as in the case of emergency night transfusions, the hospital is willing to adopt the alternative of having the recipient sign a statement releasing the hospital of responsibility in the event of the transmission of blood-borne disease. (3) The above procedures, in addition to interrupting the routine of the laboratory, delay the actual transfusion, often to the point of jeopardizing the patient's life. (4) Interns on clinical services already busy must interrupt their work to draw samples of blood from the prospective donors and later to collect blood from the donor selected. This often makes a considerable interruption in the ward routine if several donors for two or three patients come in at the same time. They usually are anxious to see the patient and oftentimes they are unwilling to wait while the typing and Wassermann tests are being performed.

These objectionable features have been eliminated at the Philadelphia General Hospital through the establishment of a central repository or blood bank for citrated blood as was suggested by Fantus.[1] We have

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followed in many particulars the organization described by Fantus but have added several details which have improved the working of the blood bank in our hands. So much interest has been shown in the bank and so numerous have been the inquiries that we have been encouraged to report the details of the system as used at the Philadelphia General Hospital.

The advantages of the blood bank idea are many: (1) Citrated blood of any type may be obtained at any time in return for a similar quantity of blood. Thus, with a supply of blood on hand at all times, blood transfusion has become almost as simple as an intravenous infusion, differing only in the preliminary typing of the recipient and in the cross-agglutination test. (2) Typing and serologic determinations on the donor's blood are performed at the convenience of the laboratory workers and as part of their routine work. No unnecessary laboratory work is done, since every type of blood drawn will be used unless it is seropositive. (3) The confusion of having numerous donors in the hospital and the irregular interruptions of the intern's ward work are avoided by a systematic routine of collecting bloods.

SOURCE OF BLOOD FOR BLOOD BANK

The source of blood continues largely to be healthy relatives or friends of the patients likely to need blood transfusions. The relatives of such patients are requested by a clinical intern to have one or more donors come to the hospital at one of the donor clinics held three times each week. The intern is requested to inform the blood bank as to the number of donors expected to come to a clinic. From fifteen to twenty-five donors contribute blood at each of the three clinics. Interns on the dispensary service are assigned to duty in the clinic, which is under the supervision of the nursing personnel of the blood bank and the surgical resident.

Other sources of blood are the house or dispensary hypertensive patients with cardiac failure, on whom therapeutic venesections are performed; and, finally, placental blood has been obtained and used in relatively few instances. In spite of the fact that a relatively large number of transfusion bloods are needed, we have rarely found it necessary to obtain blood from the patients themselves as was recommended by Fantus.

DONOR CLINIC

Clinics for receiving blood are held three times weekly, from three to five o'clock on two afternoons and from seven to nine o'clock on one evening. The blood is drawn by the interns on dispensary service who are assigned to this duty by the chief resident physician for a period of two months. The clinic is in charge of the surgical resident, and the nursing staff is provided by the supervising nurse of the blood bank. With this arrangement a fairly uniform routine of taking and handling

bloods has been developed and the advantage of having a permanent nursing personnel familiar with the procedure is obvious. The donor clinic has been set up in a room adjoining the blood bank in order to facilitate the handling and depositing of the blood specimens.

Before the blood is drawn from the donor, a tag is filled out giving his name, age, and address, the date and the name of the patient for whom the blood is being given. At the end of the venesection, the amount of blood drawn is recorded. As soon as convenient, usually within ten minutes after completion of the venesection, the blood flask, properly capped and tagged and accompanied by its tube of citrated blood, is placed in the refrigeration vault.

The vault of the blood bank is an ordinary electric refrigerator housed in the solution room of the hospital. The temperature is maintained at 39° F. Each blood type has its own shelf, and flasks not yet in circulation, i.e., awaiting type and Kahn reports, are kept in a separate section. As soon as these reports are obtained, the results are noted on the flask card and the flask is then placed in circulation on its proper shelf. The bloods in the vault are inspected daily with a flash light for evidences of bacterial growth, hemolysis or clotting. Any specimen which is regarded as suspiciously unfit is discarded. At weekly intervals, bacterial cultures are made from flasks selected at random. Care is taken not to agitate the flasks unnecessarily as it has been apparent that repeated trauma increases the tendency toward hemolysis. An effort is made to keep the reserve supply in the bank at forty flasks. This has been found adequate for a hospital of 2,700 beds where an average of forty transfusions a week are done. In general, bloods of the same type are deposited and requested with like frequencies so that no effort has been made to control the type of donors.

BOOKKEEPING

For each flask of blood placed in the bank, a 3 by 5 inch card is filled out and placed in a Rand visual index file, the visible portion of each card bearing the donor's name, the amount in the flask, and the date the blood was drawn. Space is left on this portion for recording the type and serologic reports. The file is divided into five sections, one for each blood group and one for "Unreported Types and Kahns." When the type has been determined and the serology reported negative, these data are recorded on the card, which is moved to its proper section in the file. (When the Kahn test is positive the blood is, of course, discarded.) By means of such a file, bank assets are seen at a glance.

In addition to the Rand file, a large ledger is kept, with two pages assigned to each intern. A record of the deposits is entered in the left-hand column of each page; the withdrawals are recorded in red in the right-hand column. The ledger is balanced monthly and interns owing blood are requested to make up their indebtedness.

When a flask is sent from the bank to a patient needing blood, the corresponding card is removed from the file and held pending completion of the transfusion. After the desired amount of blood has been given, the patient's nurse fills out a questionnaire covering these essentials: (1) name of patient, (2) age, (3) indications for transfusion, (4) amount, (5) time required, (6) details of reaction, if any. The patient's temperature, pulse and respiration rates are charted half hourly on the same sheet. This form, together with the apparatus, is returned to the bank, where the data are recorded on the donor's card. This card is then filed in an "inactive" file. Thus, a record of every transfusion performed is available for any future reference.

OBTAINING BLOOD FROM THE BANK

When a transfusion is to be given, the type of the patient's blood is determined and the blood bank is advised that blood of that type is desired. The card file is consulted by the supervising nurse in the bank and the card of the proper type is chosen. The flask corresponding to this card is selected and the citrated sample of blood is removed from the small cloth bag attached to the flask. Two cubic centimeters of this sample are poured into a clean Wassermann tube and sent to the laboratory with a request for cross agglutination with the patient's blood which has previously been sent for typing. The remainder of the citrated sample of blood is replaced in the bag on the flask. If the cross agglutination shows the blood to be compatible with the recipient's, a notation to that effect is made on the donor's file card and the flask with the recipient's tray is sent to the patient's ward. If the cross agglutination shows that the blood is incompatible with the recipient's, the same routine is repeated, using another blood of the same type. After a cross agglutination a flask of blood may be reserved by an intern for a period of six hours. After that period it is considered that the transfusion is no longer necessary, and the blood is again placed in the general repository.

THE TECHNIQUE OF DRAWING AND GIVING BLOOD

The introduction of a blood repository or bank in which blood is collected, stored, and administered by several individuals has made it necessary to devise a method of carrying out this procedure which would offer the fewest technical difficulties and the greatest assurance of sterility. The apparatus here to be described and the method of handling and caring for the blood have been used with such success at the Philadelphia General Hospital since the establishment of a blood bank that it seemed worth while to publish the details of the apparatus and procedure.

Since the blood was to be stored, the citrate or indirect method of transfusion was chosen of necessity and in our experience in a large num-

ber of transfusions in this hospital, there seems to be no practical advantage in the direct method of transfusion of unmodified blood over the use of citrated blood.

Apparatus for Drawing Blood.—The method of removing blood from the donor was devised so as to make the system a closed one from the vein of the donor to the receiving flask. To this end, it was determined to remove the blood by suction from the vein into a tightly stoppered graduated Erlenmeyer flask. The essential piece of apparatus is a graduated liter flask with a three-hole rubber stopper fitted with glass tubing (Fig. 1). Each of two of the stopper holes accommodates a 4 cm. length of straight glass tubing. One of these is connected by a 15 cm. section of rubber tubing to a glass adapter which fits into the needle

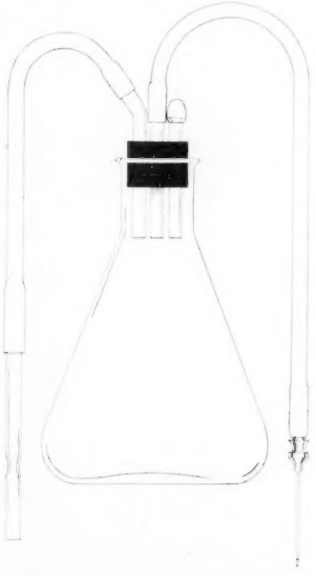

Fig. 1.—Donor apparatus.

in the donor's vein. The exposed end of the second straight glass tube is covered by a small rubber cap, such as an ordinary cystoscope tip. Through this rubber tip, anticoagulant may be injected into the flask without the loss of the partial vacuum. In the third hole of the rubber stopper is a 4 cm. length of glass tubing, the upper third of which is slightly bent. To this is attached a 15 cm. segment of rubber tubing in the end of which is a suction tip, consisting of a glass trap containing cotton or glass wool. In drawing blood, mouth suction is applied to the suction tip, thereby creating a small partial vacuum in the flask. Other equipment includes 3 towels, an 18-inch length of rubber tubing (tourniquet), Kelly hemostat, assorted needles (Nos. 21, 18, 16, 14, and hypodermic), one 2 c.c. syringe, one 20 c.c. syringe barrel fitted with a rubber (Asepto) bulb, 3 specimen tubes of 10 c.c. capacity, small cloth bag, printed tag, gauze squares, and roller bandage. This material, with

the flask and its stopper, constitutes the "donor's tray," which is autoclaved before use. Accessories not in the tray are sterile novocaine, 1 per cent, in a rubber-capped bottle, a 4-ounce bottle of sterile 2.5 per cent solution of sodium citrate, and a jar of gauze sponges immersed in 70 per cent alcohol.

Drawing Blood.—Venipuncture is executed by a doctor assisted by a nurse. The donor lies on a litter or table with the arm exposed on an arm board for six inches above the elbow. The doctor scrubs for three minutes and puts on sterile gloves. With the tray exposed, the nurse offers him the jar of alcohol sponges. Holding the sponges in the hemostat, the doctor cleanses the entire circumference of the donor's arm for a distance of six inches above and below the elbow. The arm is held elevated while a sterile towel is placed under it. On the towel is placed the rubber tube tourniquet; the arm is lowered. Sterile towels now cover the arm above and below the elbow. Using the 2 c.c. syringe and hypodermic needle, the doctor draws 1 c.c. of novocain from the rubber stoppered bottle held by the nurse and makes a wheal in the skin at the site of the proposed venipuncture. The patapar* cap is now removed from the liter flask and 20 c.c. of the sodium citrate solution are added to the flask with the 20 c.c. syringe. The syringe is now handed to the nurse who subsequently adds additional citrate as needed. With the stopper in the flask, the tourniquet is tightened, a needle of large bore, usually a No. 14, is fitted to the glass adapter and the needle inserted into the vein. Suction on the mouthpiece at this point will create a partial vacuum in the flask, and as the blood flows the flask is constantly agitated in a swirling motion. When 200 c.c. have been drawn, and if the flow appears free, a second 20 c.c. portion of sodium citrate is added. This is done by the nurse, who inserts the needle of the large syringe through the rubber tipped tube and injects the contents into the flask. She immediately refills the syringe as before. When 400 c.c. of blood are in the flask, she injects 10 c.c. more of anticoagulant. Thus a total of 50 c.c. of 2.5 per cent solution of sodium citrate has been put in the flask, enough to prevent the clotting of 500 c.c. of blood. (Interns are requested to remove not more than 500 c.c. from one donor.) While she is awaiting the completion of the procedure, the nurse removes the three specimen tubes from the tray, removes the plugs, and injects 0.5 c.c. of sodium citrate solution into one of them.

When the full complement of blood has been drawn, the glass adapter is removed from the needle and the flask set aside. The three specimen tubes are given to the doctor, who half fills each with blood flowing from the needle still in the donor's vein. The needle is now removed and a sterile dressing applied to the arm. The doctor removes the stopper

*Patapar is a vegetable parchment paper. The cap is fastened over the mouth of the flask with an elastic band before autoclaving.

from the flask and replaces the sterile patapar cap, fastening it with a rubber band. The small cloth bag is slipped over the flask and the specimen tube of citrated blood, labeled with the donor's name, is placed in it. This tube remains with the flask and is to be used for cross agglutination. The tag is filled out and tied on the flask. The remaining clotted specimens are sent to the laboratory, one with a request for typing, the other for a serologic test. The flask of blood is taken at once to the solution room where a reinforcing gauze dressing is placed over the mouth; it is placed immediately in the refrigerator.

This method of collecting blood limits as much as possible any chance contamination of the blood. Citrate may be added as needed without interfering with the partial vacuum and in this way an excess of anticoagulant may be avoided. Blood is collected separately for typing and for serologic examination, and a third marked tube containing citrated blood is attached to the flask which may be used for cross agglutination without the necessity of disturbing the stored flask.

Blood Transfusion.—For the administration of the blood an effort was made to devise a system which would permit the use of physiologic saline solution preliminary to the administration of the blood to insure an air-free system and to facilitate venipuncture. In addition, provision was sought for the following features: (1) The blood container should remain upright at all times to avoid spilling. (2) An easily readable method for judging and regulating the speed of administration should be provided. (3) Opportunity should be given for the administration of saline or glucose solution in any desired amount through the same apparatus without disturbing it.

To meet these requirements a system was devised modeled much after that described by Milroy and Matheson, of Australia,[2] in which saline solution could be given through a small trap or reservoir, to be followed by blood drawn from the flask by siphonage. The siphon withdrawal allows the blood flask to remain upright and its drop into the small reservoir permits an accurate estimation of the speed of the transfusion. A Hoffman clamp on the siphon tube is used for easy regulation of the rate of flow. Additional infusion fluid to follow the blood is poured into the original blood flask through a small glass funnel which also acts as an air vent.

In attempting to make the apparatus as cheaply as possible, the barrel of the "Triumph" type of irrigating syringe was found to be suitable for use as a small reservoir. The cone shape of the Erlenmeyer flask makes it convenient to fit on it a holder for the reservoir by using a metal ring which will rest well down on the flask.

When proper cross-agglutination results have been obtained between the patient's blood and the donor's blood removed from the citrated tube

on the flask, the flask of blood and a recipient's tray are sent to the patient's ward. The autoclaved tray which accompanies the flask of blood to the patient contains a two-hole stopper with glass tubing; a glass reservoir (syringe), with attached 30-inch length of rubber tubing and needle adapter; a metal ring to fit over flask; three towels; rubber tube tourniquet; Kelly hemostat; assorted needles (Nos. 21, 18); gauze squares and roller bandage. Accompanying the tray is a jar of gauze sponges in 70 per cent alcohol. Through the two-hole rubber stopper pass a short stemmed glass funnel and a thistle tube which reaches just to the bottom of the flask when the stopper is in place. Four thicknesses of fine mesh gauze are tied over the end of the thistle. This filter is

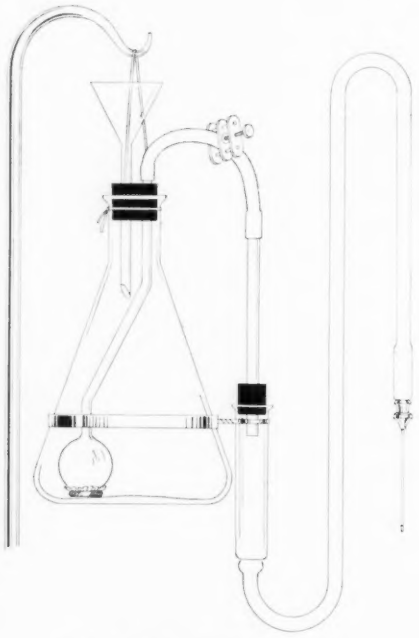

Fig. 2.—Recipient apparatus.

renewed after each transfusion. The outer end of the thistle tube connects with a 12 cm. length of straight glass tubing by means of a 15 cm. segment of rubber tubing. A Hoffman clamp is included in this section of rubber. The open end of the straight glass tube passes just through a rubber stopper which fits snugly into the Triumph syringe barrel (reservoir). (Fig. 2.)

After antisepsis of the recipient's arm in the same manner as that described for the donor's arm, and after warming the blood to near body temperature by placing the flask in water at 105° F., the metal ring is placed over the flask. (This ring is actually a double ring of metal constructed in the form of the figure 8 with one small aperture and one large one.) The covering of the flask is removed.

After the two-hole stopper is firmly inserted, the flask is suspended about three feet above the bed by means of two tapes fastened around the neck. The long section of rubber tubing attached to the reservoir is passed through the small aperture of the ring, bringing the lip of the reservoir to rest on the ring. A needle is fixed to the glass adapter at the distal end of the tubing. Warm physiologic saline solution is now poured into the reservoir, nearly filling it. After the tubing and needle have been made airfree, the recipient's vein is entered while the nurse pinches the delivery tube. When the needle is in the vein, as shown by a backflow of blood in the adapter, the tourniquet is removed and pressure on the delivery tube is released. As the level of saline solution in the reservoir falls, the rubber stopper is fitted in the reservoir. The falling head of saline solution draws blood over into the reservoir through the thistle tube, creating a siphon. As the blood passes through the gauze covering the thistle, it is filtered. The rate of flow may be adjusted by the Hoffman clamp. The siphon drip in the reservoir can be observed as readily as the flow in a Murphy drip bulb, making it easy to gauge the rate of flow. No blood is left in the flask if the thistle grazes the bottom of the flask. If it is desired to follow the transfusion with an infusion, the solution may be added to the flask through the funnel.

The advantages of this method of transfusion are several. The system is open to a minimum of contamination from without. The use of the preliminary saline solution makes it possible to clear the system of air with certainty. In addition, the transfuser may be sure that his needle is in the vein and that the flow is free before the blood flow is started. The possibility of adding other solutions without disturbing the apparatus makes it convenient to give as much fluid as desired without disturbing the needle in the vein or the apparatus. There is no pouring or dripping or spilling of blood.

Placental Blood.—Our technique of collecting fresh placental blood for use in transfusions is much the same as that recently described by Goodall and his co-workers of Montreal.[3] After the delivery of the baby, the cord is divided between two clamps in the usual manner. The maternal portion of the cord is then cleansed with 70 per cent alcohol for a distance of 8 inches proximal to the clamp. A sterile drape, measuring 40 by 18 inches, having a small hole in its center, is then placed across the perineum, and the clamped end of the cord passed through the hole for a distance of 6 inches. The cord is now cut proximal to the clamp and the blood collected in a 250 c.c. Erlenmeyer flask, to which has previously been added 8 c.c. of 2.5 per cent sodium citrate solution. The flask is agitated to insure proper citration of the blood. The flask is capped, labeled, and taken at once to the refrigerator of the blood bank. Administration of this blood as a transfusion is effected through the usual recipient's tray.

SUMMARY

A technique of blood transfusion is described for use in connection with a blood bank. It has the following features:

1. A nearly closed system offering minimal chances of contamination.
2. Blood is drawn into, stored in, and delivered from a single flask.
3. The drawing of blood is facilitated by means of suction.
4. Sodium citrate is added to the flask as the blood enters, thus avoiding too high a concentration of anticoagulant.
5. Administration of the blood is preceded by a small saline infusion, whereby the tubing is cleared of air and which permits accurate placing of the needle in the recipient's vein before the blood is allowed to run.
6. The apparatus used is described in detail.
7. A technique for collecting placental blood is described.

RESULTS IN 1,000 TRANSFUSIONS USING CITRATED REFRIGERATED BLOOD

The data here presented are based upon our experience in the first 1,000 transfusions given through the agency of the blood bank. In order to provide 1,000 usable specimens of blood, blood was drawn from 1,123 donors. Amounts of blood varying from 250 to 600 c.c. were obtained, the average quantity being about 450 c.c. The incidence of each blood group is shown in Table I.

TABLE I

INCIDENCE OF BLOOD GROUPS IN 1,123 DONORS

Type I*	3.3%
Type II	32.2%
Type III	15.0%
Type IV	49.5%

*Moss classification

One hundred and twenty-three specimens of blood (11 per cent) were not used for transfusions. The reasons for this loss are given in Table II. Those marked unsuitable laboratory specimens are those in which an insufficient quantity of blood was drawn, where the specimen hemolyzed rapidly or where a specimen which was sent for serologic testing had been citrated by mistake. It was interesting to note that only 25 of the 1,123 deposits (2.2 per cent) were discarded because of age. Speci-

TABLE II

SOURCES OF LOSS IN BANKING 1,123 BLOODS

	NUMBER	PER CENT
Seropositive	53	43
Unsuitable laboratory specimens	20	16
Aged	25	20
Hemolyzed	17	14
Cultured	6	5
Broken	2	2
Total	123	100

mens were discarded when they had remained in the refrigerator for 5 weeks. The average flask of blood remained in the refrigerator for 5 days before its use for transfusion. Naturally the preservation time was shortest in the commoner blood groups; the flasks in Groups II and IV were usually called for and used for transfusion within 24 to 48 hours after they were placed in the refrigerator. On the other hand, the bloods discarded because of age were almost exclusively of Group III.

Regarding hemolysis, it appears that this tendency is unpredictable and is entirely an individual variable. Some specimens showed beginning hemolysis as early as 2 days after withdrawal. Many others showed no evidence of hemolysis at the end of 7 weeks of refrigeration.

Cultures made from blood specimens taken at random from the refrigerator have been consistently negative. In addition, cultures made from blood remaining in a flask following transfusion reactions likewise have been negative with two exceptions. One of these showed a growth of *Staphylococcus aureus*. The other resulted in a growth identified as *Streptococcus viridans* and a diphtheroid bacillus. In both of these cases in which positive cultures were obtained, the flasks were open to contamination before the cultures were made, having stood open and unprotected throughout the night and having been freely manipulated by unsterile hands.

The incidence of reaction has been relatively low (7.4 per cent). We have classified the reactions as mild, severe, and allergic. A mild reaction is one which is accompanied by a temperature not exceeding 101° F., at times associated with a feeling of chilliness and vague unrest. A severe reaction is manifested by a temperature elevation of over 101° F., a frank chill, a decrease in pulse volume, and an increase in pulse rate. An allergic reaction presents chiefly urticarial phenomena, occasionally with a slight temperature elevation, and rarely with a chill. The frequency of these untoward results of transfusion is tabulated in Table III. We have not noted any increase in the frequency of reactions in blood which has been refrigerated for longer periods of time (2 to 3 weeks).

TABLE III

REACTIONS IN 1,000 TRANSFUSIONS USING CITRATED REFRIGERATED BLOOD

	NUMBER	PER CENT
Mild	29	2.9
Severe	28	2.8
Allergic	17	1.7
Total	74	7.4

SUMMARY

We have described in detail the routine of the working of the blood bank of the Philadelphia General Hospital. The advantages of the bank idea are many. The source of the blood is usually healthy relatives of patients. Blood is drawn at regular donor clinics and im-

mediately deposited in a refrigerator. The bookkeeping of the bank has been described.

The technique of an almost closed system for the use of the citrate method in the blood bank has been described.

The results in 1,000 transfusions given by the method described have been analyzed. In giving 1,000 transfusions, blood from 1,123 donors was drawn. Eleven per cent of these were not used for transfusion.

Reactions occurred in 7.4 per cent of the 1,000 transfusions.

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OPERATION FOR DISLOCATED SEMILUNAR BONE OF THE WRIST

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DISLOCATION of the semilunar bone, while not extremely rare, is an injury more frequently overlooked than correctly diagnosed. The purpose of calling attention to this lesion again is threefold: the fact that the interpretation of findings by the surgeon or roentgenologist is frequently incorrect, leading to a deficient diagnosis; to emphasize the clinical and roentgenologic diagnostic features, each of which is typical; and third, to show that the proper method of treatment, if reduction by manipulation fails, is open operation with replacement of the bone in its normal location, not excision of the semilunar bone. One of us (H. R. M.) has seen 5 cases since 1933 which have been diagnosed mistakenly by one or more doctors before the lesion was recognized. In the records of patients admitted as in-patients to Charity Hospital since 1926, there are 15 cases with a diagnosis of dislocation of the semilunar bone. Cases reduced in the emergency service and sent to the clinic as out-patients are not included in this.

In the Tulane Fracture Clinic of Charity Hospital, which includes only part of the white male fracture service, there have been 649 cases treated during the last two years. Among this group there were 2 cases of dislocation of the semilunar bone; an incidence of 1 in 325 cases; 3 cases of fractured scaphoid of the carpus, 2 of which were associated with the above dislocations.

Of the 15 cases with dislocated semilunar bones admitted to the hospital since 1926, 13 were males; 2 were females. In 9, fracture of the carpal scaphoid was associated with dislocated semilunar. Of 5 cases operated upon by one of us (H. R. M.) and reported herein, 4 (80 per cent) had an associated fracture of the scaphoid. A fracture of the carpal scaphoid is more often correctly diagnosed than a dislocated semilunar bone by the inexperienced surgeon, and, if both lesions coexist, the dislocated semilunar may be overlooked even though the fractured scaphoid is recognized. Once we encountered a case subsequent to the removal of the proximal fragment of a fractured scaphoid as a procedure of election by another surgeon, who had overlooked the dislocated semilunar with which the fractured scaphoid was associated.

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The type of injury causing dislocation of the semilunar bone was recorded in 12 of the 15 cases as follows: direct blows on the back of the hand, 5; falls, presumably on the outstretched hand, 4; automobile accidents in which the exact mechanism was not explainable by the patient, 3; no history of the type of injury was recorded in 3 instances. The importance of the type of injury producing this lesion has been grossly overemphasized. Presumably from the displacement of the bone anteriorly it has been reckoned that the injury is the result of hyperextension of the hand, the head of the capitate squeezing the lunate forward and breaking the posterior radiolunate ligament. This, however, is presumptive and, as in many other fractures, certain authors apparently get assistance in revealing to themselves the type of trauma from the lesion, rather than assistance in diagnosing the lesion from the type of trauma. In the production of dislocation of the semilunar bone, the injury apparently can be of several varieties; thus, in the 15 cases hyperextension is recorded with reasonable certainty only in 4 instances; whereas, direct injury on the dorsum of the wrist is recorded in 5. If one is careful in questioning the patient about the direct mechanism of injury, it will be proved conclusively that not 10 per cent of the patients can give the story of the details of an accident with even the slightest degree of certainty. These lesions can as well be diagnosed accurately with the story that the patient has hurt his wrist, as when the mechanism is indicated by the patient as being a fall on the outstretched hand or a blow on the back of the wrist.

Characteristic clinical features of dislocations of the semilunar bone are as follows: The wrist appears thickened anteroposteriorly. There is a prominence on the volar surface. The increase in anteroposterior diameter is greater than can be attributed to the soft tissue swelling. Moreover, the prominence of the wrist is resistant, not compressible. The fingers are held paralytically in slight flexion, and, because of pain, there is very little motion in the hand and wrist. (Figs. 2 and 5.) Attempts at motion result in so much pain that 15 degrees of flexion or extension of the fingers or wrist may be the limit, particularly in recent injuries. Radial and ulnar deviations of the hand are likewise limited. There may or may not be subjective numbness and obtunded sensation over the index and middle fingers and the radial side of the fourth finger due to pressure on the median nerve. Even in old cases the patient complains of weakness of the hand and wrist and the grip is extremely weak. Over the carpus anteriorly is found a resistant prominence and posteriorly just distal to the radius an abnormal fossa might be palpable, though it may not be visible due to swelling. Pressure in the anatomic snuffbox may reveal exquisite tenderness which suggests that, together with the dislocation of the semilunar bone, there is a fracture of the carpal scaphoid. The three main features of the objective findings in dislocated semilunar are: (1) the increased promi-

nence of the wrist anteriorly; (2) characteristic position of the hand, with the wrist held straight and the fingers slightly flexed and relative immobility in this position; and (3) the palpable prominence of the semilunar bone anteriorly under the anterior carpal ligaments. The characteristic appearance of thickened straight wrist and slightly flexed painfully fixed fingers is almost diagnostic. None of these findings, however, will leave full assurance of the correct diagnosis without the x-ray.

Roentgenograms reveal the true diagnosis in a suspected dislocation of the semilunar bone. The anteroposterior view may show overlapping of the semilunar and the head of the os magnum, or the semilunar may be displaced more extensively as is shown in Fig. 3. The lateral view of the normal wrist shows very distinctly the head of the os magnum fitting into the concavity of the semilunar with the semilunar convexity articulating with the radial articular surface. This lateral roentgenographic view reveals the conformity from which the bone received its name. In dislocation of the semilunar, lateral roentgenograms show the bone displaced anteriorly with a concave surface usually pointing forward and the convexity jutting against the head of the os magnum. The bone is generally so close to its normal position, however, that the inexperienced eye may overlook a perfectly obvious dislocation. To one who has not seen the lesion previously it can be discerned only by being aware of the possibility of its presence and looking for the normal relations. Occasionally the semilunar will be displaced widely. In such instance it may be found above the lower margin of the radius and above the anterior annular ligament of the carpus (Fig. 3). Dislocation of the semilunar bone itself is more common than posterior dislocation of the head of the os magnum, in which instance the semilunar retains its normal relationship to the radius. The proximal fragment of a fractured scaphoid is frequently dislocated forward with the lunate. This occurred in two of our five cases. Such a dislocation is simultaneously and spontaneously replaced when the lunate is reduced even though the reduction be by open operation. Other fractures, notably that of the radial styloid may occur with dislocated semilunar. This happened twice in our five operated cases. In one case the base of the fourth metacarpal was fractured. Whenever a dislocation of the semilunar is found, the scaphoid bone should be carefully inspected in the roentgenogram to determine if a fracture of this bone is coexistent, because, as demonstrated by the figures presented, an associated fracture may be found in from 50 to 80 per cent of the cases. Oblique views may show some fractures of the scaphoid more clearly. Fracture of the scaphoid necessitates more prolonged immobilization after reduction than if the semilunar dislocation is uncomplicated.

TREATMENT

Several methods have been advocated for reducing dislocations of the lunate bone. All reductions of course are attempted under anesthesia. The methods deserving mention are: (1) Hyperextension of the hand, with pressure by the operator's thumb on the lunate distally and backward to re-engage the posterior lip of the semilunar under the head of the os magnum. When this is accomplished, the hand is flexed and then put into a position of optimum function for immobilization. The Thomas wrench has been recommended for hyperextension. A modification of this method is the use of a broom handle, rolling it distally across the volar surface of the wrist while the hyperextended hand is slowly flexed, at the same time exerting traction distally on the fingers. This procedure is not recommended because it is likely to traumatize the structures severely without accomplishing reduction. Proof of complete reduction must be obtained by the roentgenogram. (2) In a second method the operator hyperextends the hand and presses distally on the dorsum of the patient's hand at the head of the os magnum to increase the distance between the radius and os magnum. The semilunar bone is pressed backward and distally by the operator's other thumb. After the head of the os magnum slips over the posterior lip of the semilunar bone and into its concavity, the hand is flexed and immobilized in a neutral position. (3) Böhler[1] recommends traction in the longitudinal axis of the arm, on the thumb and fingers, with the patient under deep anesthesia, continuing the traction for a period of at least ten minutes. When the space between the capitate and radius is increased sufficiently, the flexor tendons press the semilunar back into position. (4) Open reduction; and (5) excision.

In very recent cases reduction by manipulation under anesthesia is almost always obtainable. However, after a period of a few days or weeks, when the reaction to trauma has begun to firmly establish new conditions, reduction by manipulation, even under deep anesthesia, may be difficult or impossible. Numerous rough attempts at closed reduction should not be persisted in as the open operation can accomplish reduction with certainty and with less trauma. Unfortunately many authors and many more operators consider an unreduced semilunar bone a prize to be removed, stating that function after removal of the semilunar will be almost as good as if the semilunar were in place. Function is never as good as if the semilunar is accurately replaced, and replacement can be accomplished by an open operation. In almost all instances the posterior ligament between the radius and lip of the semilunar bone is torn, but the anterior ligament remains intact. As has been shown by Conwell,[3] as well as by our series, replacement of the bone results in no subsequent atrophy or disturbance

of calcification. Even if the semilunar bone is found at operation to be entirely unattached to any tissue, until it is proved otherwise, replacement seems better than removal.

THE OPERATION

Beginning proximal to the proximal transverse furrow on the anterior surface of the wrist and between the tendon of the palmaris longus and flexor carpi radialis, an incision is made which runs distally for a distance of approximately 4 cm. onto the hand just to the ulnar side of the tuberosity of the scaphoid (Fig. 4). The anterior annular ligament is incised and the flexor sublimis and flexor profundus tendons are displaced together with the median nerve to the ulnar side. The dislocated semilunar bone will be found as a prominence and the concave glistening articular surface will be easily recognized. After incising the fibrous tissue over the carpal bones between the scaphoid and os magnum, the head of the os magnum becomes clearly visible as the semilunar is rotated forward. A curved periosteal elevator is inserted under the head of the os magnum while hyperextending the hand. Pressure on the posterior lip of the semilunar with a blunt pointed elevator while the head of the os magnum is being elevated will allow the bone to recover its normal position, with relation to the radius and os magnum. After the periosteal elevator is removed, the head of the os magnum engages in the concavity of the semilunar. This relatively simple procedure completes the operation except to close the anterior annular ligament, the subcutaneous tissue and skin, with interrupted silk sutures. The wound is dressed with xeroform gauze (gauze impregnated with 5 per cent xeroform powder in white vaseline), and the hand is immobilized with a skin cast extending from metacarpophalangeal joints to the upper third of the arm. Immobilization is continued for approximately three weeks if a dislocation alone exists; for eight weeks if there is an associated fracture of the scaphoid.

The abstracts of the case histories of the five cases operated upon by one of us are as follows:

CASE 1.—F. V., white male, aged 42 years, was admitted to Charity Hospital on June 13, 1933. On June 10, while repairing an automobile, an engine block slipped off a jack and fell on his hand. His hand pained him severely; more toward the radial side of the wrist. He was seen in the accident room where a diagnosis of Colles' fracture was made. He was not admitted to the hospital until three days later. X-ray showed fracture of proximal and fourth metacarpals and the styloid process of the ulnar and anterior dislocation of the left semilunar carpal bone. The left wrist was markedly swollen. There was a small laceration between the fourth and fifth knuckles on the dorsum of the hand, and marked impairment of motion of the wrist. No evidence of deformity was described. An attempt at closed reduction made on June 15 failed. Open reduction was done on June 17, seven days after the accident. The operation described above was performed, with replacement of the semilunar bone (Fig. 1). However, catgut was used instead of silk which we

now employ. Subsequently the man had an uneventful convalescence and recovered perfectly. He is now driving a moving van with no impairment of motion whatsoever in his wrist and no weakness or pain.

CASE 2.—H. L., aged 27 years, a white male, was admitted to the hospital on Jan. 3, 1935. On Nov. 26, 1934, he was struck on the back of the left hand with a chair. He had pain for two weeks constantly and after then at intervals and at night. He had been unable to use his hand and any wrist motion caused pain. Diagnosis

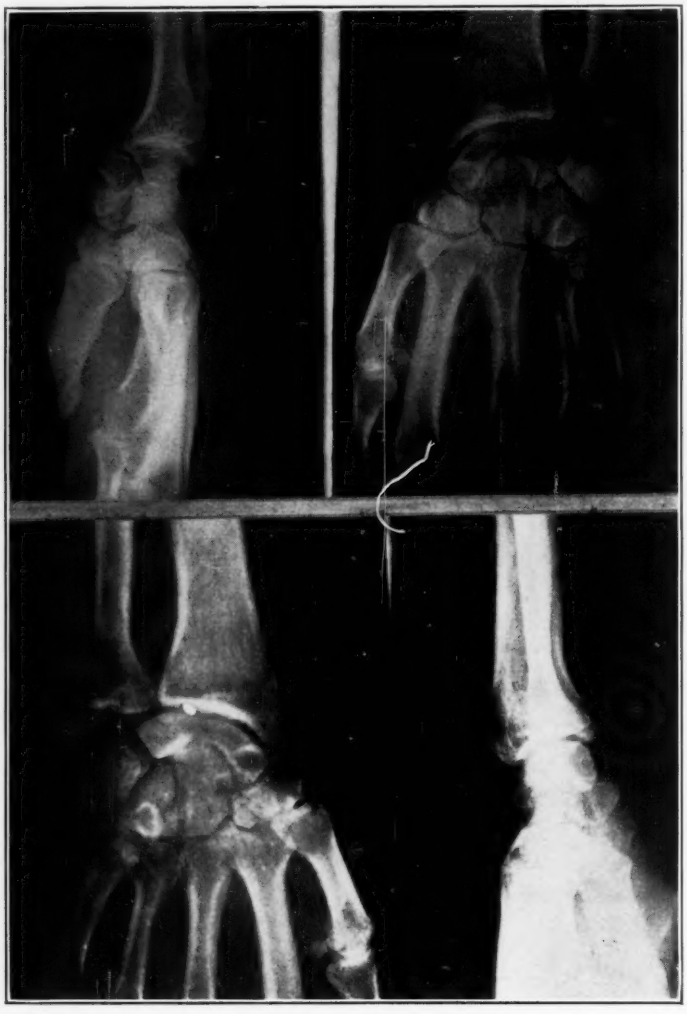

Fig. 1.—Dislocation of the carpal semilunar bone with associated fractures of the fourth metacarpal and styloid process of the ulnar (Case 1). *Above*, showing the semilunar dislocated with the concavity turned sharply forward; *below*, after operative replacement. The head of the os magnum fits into the concavity of the semilunar. Note that the fracture of the fourth metacarpal is united.

had not been made before the patient's admission to the hospital. Examination showed swelling and prominence anteriorly on the wrist. The hand was held in extension, the fingers slightly flexed; voluntary motions of the fingers and the hand were extremely slight. Roentgenograms of the left wrist showed a dislocation of the semilunar bone and a fracture of the scaphoid. No attempt at closed reduction was made because of the lapse of time since the injury. The operation described above

was performed six weeks after the initial injury, and the semilunar bone was replaced. A skin cast was applied and immobilization was continued for eight weeks. Subsequent x-rays showed the bone to be in good position with union of the fractures of the scaphoid and the styloid of the ulnar (Fig. 2). This patient had complete recovery of function without any residual disability whatsoever.

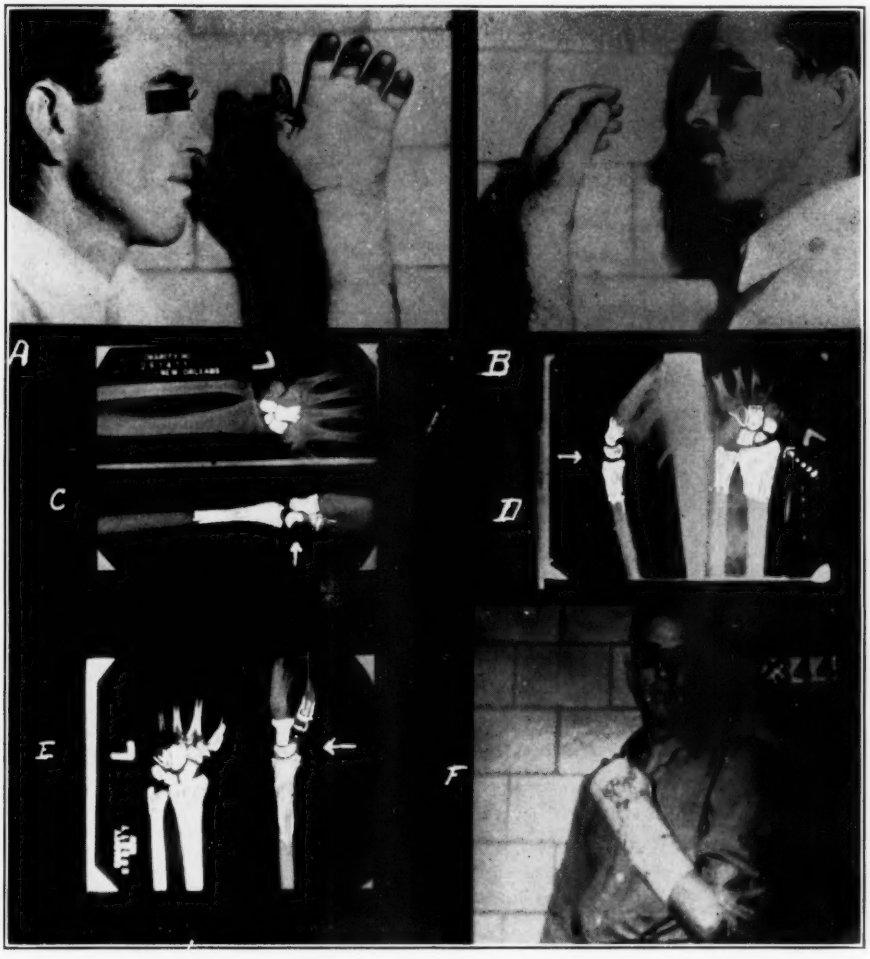

Fig. 2.—(Case 2.) *A* and *B*, Appearance of the hand before reduction of dislocation of the carpal semilunar bone. The wrist is thickened at the carpus and the fingers are held in slight flexion with a relatively straight wrist. Because of pain there is very little motion of the fingers or wrist. *C*, Retouched x-ray showing the concavity of the semilunar bone turned forward and the head of the os magnum posterior to its normal position. There is a fracture of the scaphoid. *D*, After operation, showing the head of the os magnum fitting into the concavity of the semilunar. Because of ulnar deviation of the hand, the fragments of the carpal scaphoid are widely separated. *E*, Radial deviation of the hand has approximated fragments of the scaphoid which are now united. *F*, Patient shown in type of cast used for immobilization, which should be continued for eight weeks if there is an associated fracture of the carpal scaphoid.

CASE 3.—L. A., aged 33 years, white male, was admitted to Charity Hospital Oct. 8, 1936. Eighteen months previously he had fallen from a scaffold and hurt his wrist. He had continued to have pain in the wrist and weakness of his hand, but, though numerous doctors had seen him, the correct diagnosis had not been made. Examination at the time of admission to Charity Hospital showed limitation

of motion of the wrist in all directions and weakness of the grip. There was a prominence anteriorly on the carpus, which, on pressure, caused marked pain which radiated distally into the index and middle fingers. Roentgenograms showed dislocation of the semilunar bone and fracture of the scaphoid. Though the bone had been out of position for eighteen months, replacement was attempted at open operation. It was possible to engage the head of the os magnum in the concavity of the semilunar, but it was impossible to hold it in this position without flexing the wrist. Flexion of the wrist was maintained for a period of eight days during which time x-rays showed the head of the os magnum to be in the concavity of the semilunar. Extension of the hand, however, after eight days resulted in redislocation of the semilunar bone. The semilunar was subsequently removed. There was slight improvement following this, particularly in the disappearance of the shooting pain which the patient previously had on pressure over the carpus and in the numbness which had persisted prior to excision of the bone. Function, however, was never

Fig. 3.—An unusual case of dislocation of the carpal semilunar bone (case of Dr. H. Theodore Simon). Such wide displacements are uncommon but occasionally do occur. The procedure of choice is not excision of the semilunar bone, but replacement either by manipulation or by open reduction.

good. The patient worked as a longshoreman prior to injury, but has not been able to do hard work with the hand since. He still complains of weakness of his hand and tenderness over the carpus. Motions are limited in all directions.

CASE 4.—C. U., aged 19 years, a white male, admitted to the Charity Hospital May 17, 1937. On May 16, 1937, he was hurt in an automobile accident, and had pain in both arms. He had been treated elsewhere for lacerations and bruises and his right arm was in a splint. Removal of the splint showed swelling of the fingers and the hand, tenderness at the lower end of the radius with marked limitation of motion in the wrist. X-ray showed fracture of the scaphoid with displacement and overlapping of the fragments and anterior dislocation of the semilunar bone. Open operation was done after attempts at closed reduction failed. The semilunar bone was replaced as described above and likewise simultaneously the fragments of the fractured scaphoid came into accurate position. Subsequent x-rays showed union of the navicular fracture and the lunate bone to be in good position without evidence of atrophy. The patient made an uneventful recovery and had no residual disability whatsoever.

CASE 5.—B. H., aged 57 years, a white male, was admitted on Feb. 16, 1938. On Jan. 8 he had been hit on the back of the hand by a crank while he was cranking a car. The handle swung around and hit him on the back of the hand. Pain was not severe. The next day he went to the hospital. He had a splint applied. The emergency officer, apparently not sensing the type of injury, did not have an x-ray taken. He was told to return in three weeks. He returned after that time to the

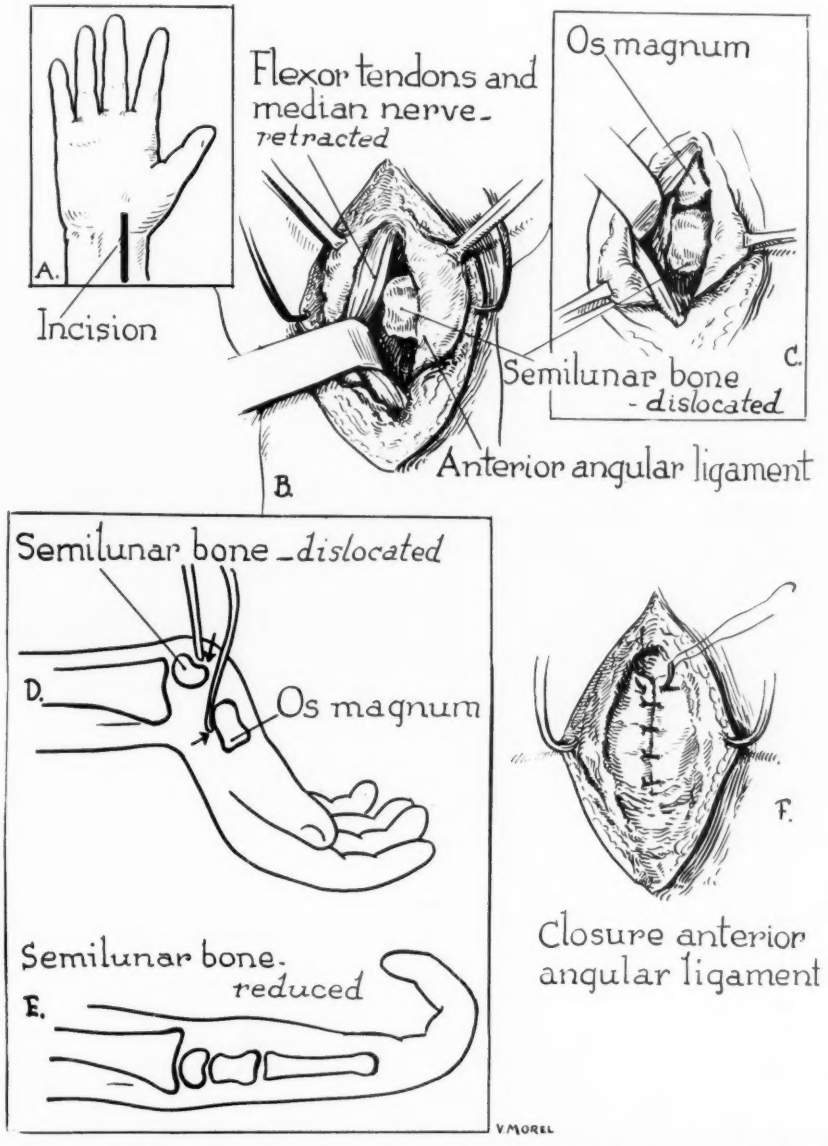

Fig. 4.—Operation for replacement of a dislocated semilunar bone irreducible by manipulation. *A*, The line of incision is just to the ulnar side of the tendon of the flexor carpi radialis. *B*, After incising the anterior annular ligament, the flexor sublimis and profundus tendons with the undisclosed median nerve are retracted to the ulnar side. This exposes the glistening concavity of the dislocated semilunar. *C*, The capsular fibers overlying the os magnum are incised, exposing the smooth head of the os magnum. *D*, With the hand hyperextended and with the aid of a curved elevator the head of the os magnum is elevated while pressure is made posteriorly on the distal (posterior) lip of the dislocated semilunar. *E*, The position when the bone has been reduced. *F*, The annular ligament and wound are closed with interrupted silk sutures.

Fig. 5.—(Case 5.) *A*, Shows the patient with characteristic appearance of the hand with dislocation of the carpal semilunar bone. The wrist is thickened and the fingers are held in slight flexion with very little motion as is also shown in Fig. 2. Such an appearance is characteristic of dislocated carpal semilunar bone. *B*, The x-rays before and after open operation and replacement of the dislocated semilunar. The semilunar bone is shaded. In the preoperative view the convex head of the os magnum is seen behind the displaced semilunar: whereas, in the postoperative view, the head of the os magnum fits in the concavity of the semilunar. Note that the displaced fragment of the fractured scaphoid is in good position in the postoperative x-rays. X-rays have been slightly retouched to insure clarity. *C*, The patient's hands after full recovery. There is no residual disability. Note the scar of the incision indicated by arrows.

clinic. Objective findings showed swelling, especially of the wrist, with a prominence anteriorly. The hand was held in extension with pitifully little motion of the wrist and fingers. Motion caused pain. He could flex fingers to 30 degrees only. The thumb could scarcely be moved at all. On the anterior surface proximal to the thenar eminence was a hard immovable mass about the size of an almond. X-rays showed dislocation of the semilunar bone anteriorly and a fracture of the scaphoid. An open reduction was done as described five weeks after the accident. The bone was replaced and immobilization was continued for eight weeks (Fig. 5). Union of the scaphoid followed promptly. He had an uneventful convalescence and complete range of motion and full function returned.

SUMMARY

It is thus shown that of 5 cases in which the semilunar bone was replaced by open operation, 4 in which the operation was done within a reasonable time (longest, six weeks after the injury) had perfect results. The fifth case, in which the dislocation had existed for eighteen months, had a poor result and the semilunar bone had to be removed. If reduction of the dislocation of a semilunar bone of the wrist cannot be accomplished by manipulation, open operation is indicated with replacement of the bone in its normal position, not removal of the bone.

The clinical and roentgenologic features of the lesion are described.

An operation for replacement of the dislocated semilunar is described.

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THE EFFECT OF EXPERIMENTAL HYPERTHYROIDISM AND HYPOTHYROIDISM UPON THE CONCENTRATION OF CHOLESTEROL IN HEPATIC BILE*

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CONSIDERABLE evidence has been presented in the literature to show that the formation of gallstones is preceded or accompanied by hypercholesterolemia. For example, Boyd[1] has reported hypercholesterolemia during the latter months of pregnancy, a condition in which the first symptoms of gall-bladder disease are very frequently manifested. Moreover, data from this laboratory[2] indicate that the cholesterol concentration in the gall-bladder bile of pregnant women at term is above normal. Among others, Fowweather and Collinson[3] and Bockus, Willard, and Metzger[4] report that gallstone disease is frequently accompanied by a hypercholesterolemia.

These studies carry with them the implication that a high blood cholesterol level affects the concentration of cholesterol in the bile, either by increasing the cholesterol in the hepatic bile or by adding cholesterol to the bile in the gall bladder.

Opposed to this theory are the findings of other workers. Andrews,[5] Campbell,[6] and Ravdin,[7] for example, have found that gallstone disease is not commonly accompanied by hypercholesterolemia. This, of course, does not rule out the possibility that a high blood cholesterol might have existed at the time stones were first formed. Gardner[8] reported that autopsies on a group of patients dying from lipoid nephrosis, a condition in which the blood cholesterol is very high, showed that gallstones had not occurred in these cases.

It seemed that, before any conclusion could be drawn as to the relationship between hypercholesterolemia and gallstone formation, it was necessary first to determine whether the level of cholesterol in the blood had any influence on the amount of cholesterol in the bile. Since it is recognized that changes in the blood cholesterol occur in hyperthyroidism and hypothyroidism and because these conditions can be experimentally produced in animals, it was decided to study the cholesterol in the blood and hepatic bile of biliary fistula dogs during the experimental production of these conditions.

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EXPERIMENTAL

Normal dogs on the routine animal house diet were used in these experiments. Biliary fistulas were prepared by cholecystectomy and double intubation of the common duct by a method previously described.[9] With this method, samples of hepatic bile could be collected when desired, or the two tubes could be connected and the bile allowed to flow into the duodenum. The operations and aftercare of the wounds were done with due regard to aseptic precautions. The animals were divided into four groups:

1. Four animals served as controls. These received no further treatment. Bile was collected at intervals and analyzed for cholesterol concentration.

2. The second group consisted of four dogs to which desiccated thyroid extract was fed. The dose varied from 10 to 30 gm. a day. The total dosage varied from 300 to 550 gm. At intervals, the blood cholesterol was estimated and twenty-four-hour bile samples were collected for cholesterol determinations.

3. In the third group four dogs were given from 50 to 90 mg. of thyroxin* intravenously over a period of from five to ten days. Cholesterol analyses of the blood and bile were made at intervals during the experiment.

4. In the fourth group four dogs were subjected to a total thyroidectomy in addition to the biliary tract operation. In two of the dogs the total thyroidectomy was performed after the biliary fistula was established, while in the other dogs the thyroidectomy was performed about three weeks before cholecystectomy and double intubation of the common duct. Here, again, blood samples and twenty-four-hour bile samples were analyzed for cholesterol.

The cholesterol determinations were made by the colorimetric method of Autenrieth and Funk, as described by McMaster.[10]

RESULTS

In Fig. 1 are shown the hepatic bile cholesterol concentrations and total twenty-four-hour output at intervals on four normal dogs. The cholesterol varied from 4.6 mg. per 100 c.c. to 56 mg. per 100 c.c.; while the total twenty-four-hour output varied from 5 mg. to 54 mg.

Fig. 2 shows the results of feeding four dogs desiccated thyroid for considerable periods of time. There was no change in the bile cholesterol that could be attributed to the thyroid feeding. It will be seen that, although the blood cholesterol fell considerably as the result of the thyroid feeding, there was no significant change in the cholesterol concentration, or total cholesterol output in the bile, the variation being approximately the same as in the group of control dogs.

*The thyroxin used in these experiments was kindly furnished by Eli Lilly and Company.

In Fig. 3 are given the results following the administration of thyroxin intravenously to four dogs. Dog 414 was given 90 mg. of thyroxin intravenously in nine days. He died an apparently thyrotoxic death with a blood cholesterol concentration of 40 mg. per cent. Dog 672 received 70 mg. of thyroxin in seven days and the blood cholesterol concentration fell to 70 mg. per cent. Dogs 681 and 684 had no significant fall in the blood cholesterol concentration, although they each received

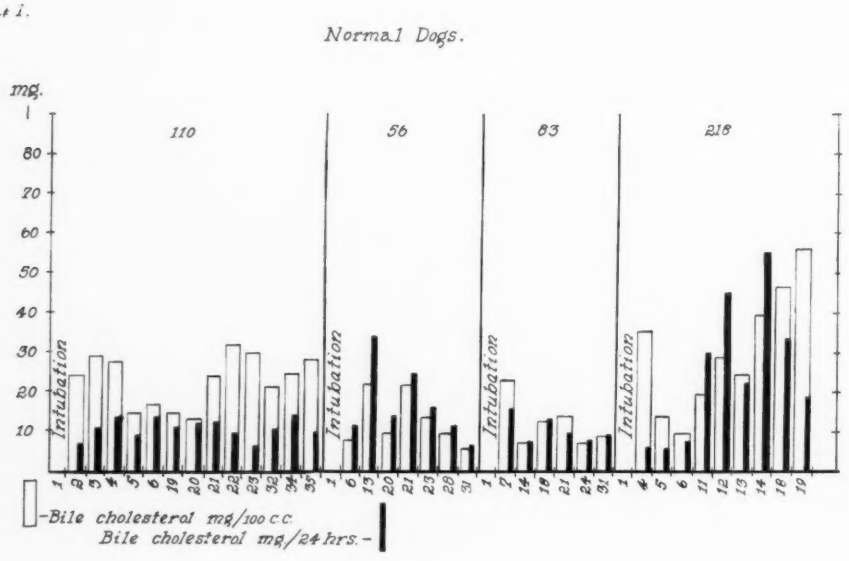

Fig. 1.

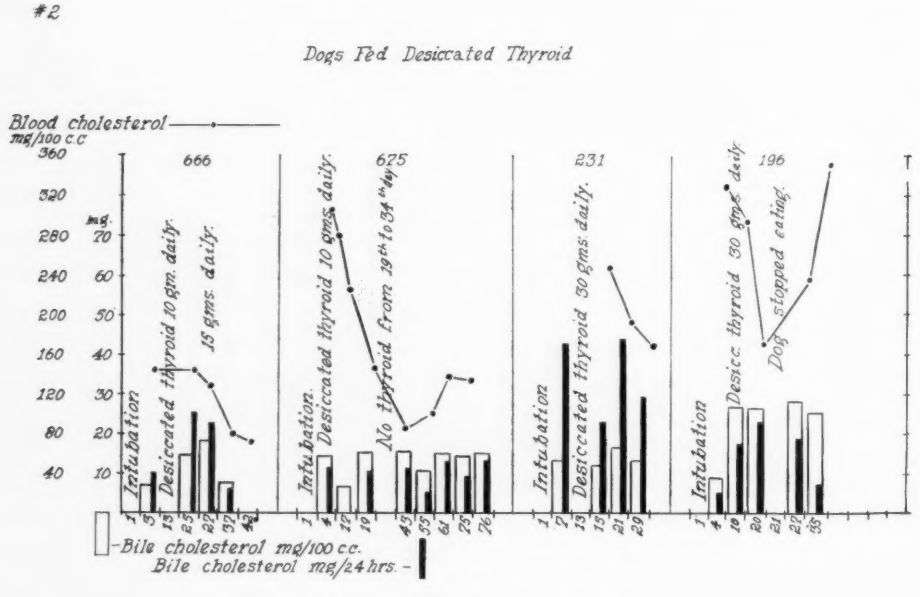

Fig. 2.

50 mg. of the thyroxin intravenously and were probably thyrotoxic. Examination of the bile cholesterol concentrations reveals no significant variation from the controls as the result of thyroxin administration.

In Fig. 4 are shown the results of the efforts to produce hypothyroidism. In Dog 655 the blood cholesterol concentration rose to 363 mg. per cent. In none of the dogs was there a significant variation in the bile cholesterol concentration from the normal values.

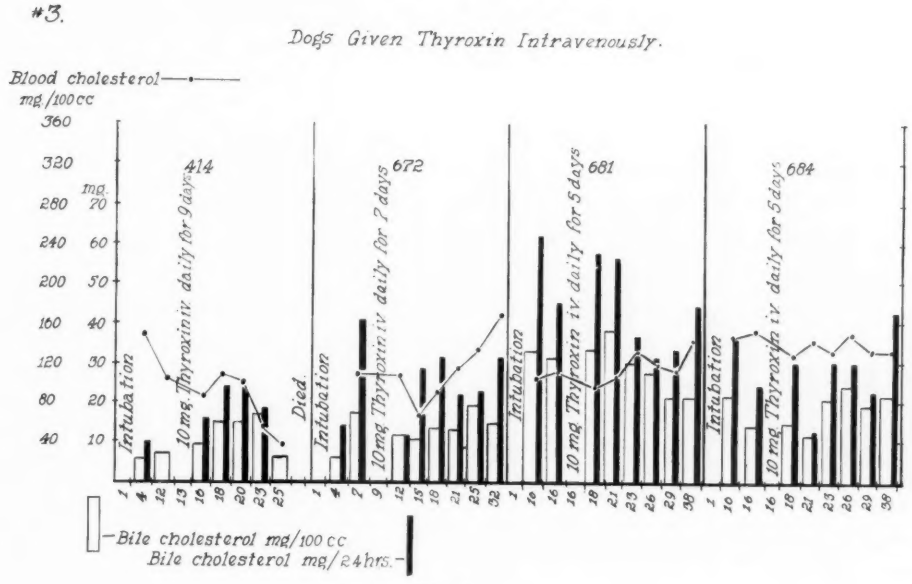

Fig. 3.

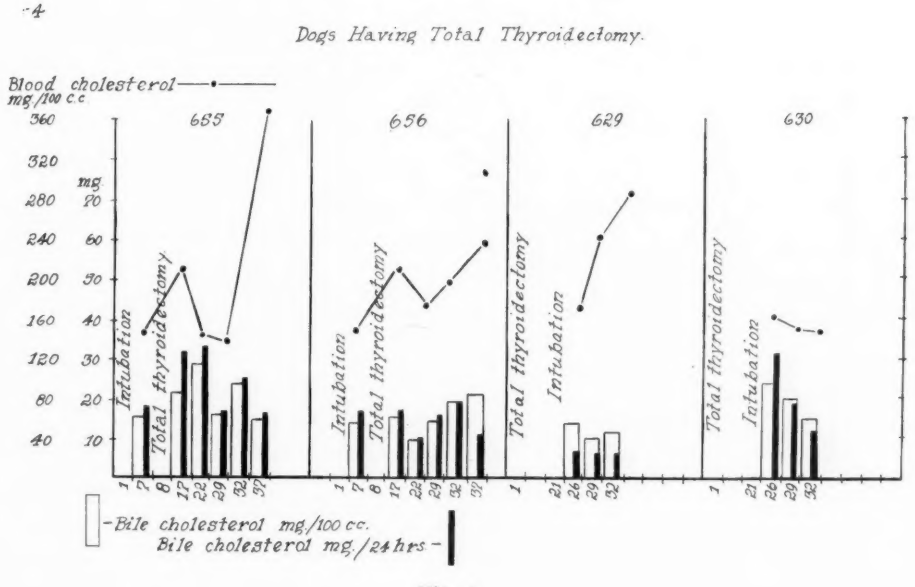

Fig. 4.

DISCUSSION

It is obvious from the data in Fig. 1 that the variation in cholesterol concentration in the hepatic bile of the normal dogs is considerable. Such variations have also been reported by McMaster.[10] Any change in the bile cholesterol produced by our experimental methods, therefore, would have to be constant and considerable to be significant. We would consider that, if after the administration of thyroxin or after total thyroidectomy, the bile cholesterol concentration or total bile cholesterol output reached either a high or low value and remained so throughout the experimental periods, the effect could be attributed to the experimental condition and, therefore, would be significant. If, however, the bile cholesterol continued to show the same daily variations at approximately the same level as in the normal animals, it could be assumed that the variations in the blood cholesterol concentrations were without effect on the bile cholesterol concentration under the conditions of our experiment.

It may be questioned, of course, whether the animals used in these experiments were hyper- or hypothyroid. It has been previously demonstrated that hyperthyroidism[11] and hypothyroidism[12] may be produced experimentally by the methods used in these experiments, and the collateral picture in these animals suggested that such states were produced. No basal metabolic rate determinations were made, since we were interested in the relationship between the blood and bile cholesterol concentrations and used the hyper- and hypothyroid states to produce the conditions we desired.

Only a few papers have been published concerning the relationship of the thyroid to bile cholesterol, but, even so, the data are conflicting. Wilkinson[13] and Hurxthal and Hunt[14] reported findings on bile from human patients, indicating that in hyperthyroidism and hypothyroidism the bile cholesterol concentration varies inversely with the blood cholesterol concentration. Unfortunately their figures for bile cholesterol, except in a single instance, are based on the analysis of material obtained by duodenal drainage and in that instance it was not stated whether the bile was obtained from a common duct or gall-bladder fistula. Analyses of duodenal contents for cholesterol, of course, do not give an accurate idea of the amount or concentration of cholesterol in the hepatic bile.

Leites and Isabolinskaja,[15] however, working with dogs with gall-bladder fistulas, reported an increased cholesterol concentration in bile after an injection of 1 mg. of thyroxin subcutaneously. On the other hand, Besuglow and Tutkewitsch,[16] using the same experimental method, reported a fall in the cholesterol concentration of the bile after the injection of 2 mg. of thyroxin and a rise after total thyroidectomy. Blood

cholesterol determinations were not made in these experiments. Parhon and Werner[17] reported findings similar to those of Besuglow and Tutkewitsch, but did not give the method used.

In our experiments we were unable to demonstrate any significant variation in the concentration or total amount of cholesterol in the bile, with alterations in blood cholesterol produced by experimental hyper- or hypothyroidism. This is in agreement with other experiments carried out in this laboratory[7] in which cholesterol was fed to patients in amounts sufficient to raise the blood cholesterol without having any appreciable effect on the concentration of cholesterol in the bile. It was previously determined that the bile contained sufficient bile salts to maintain the cholesterol in its normal state.

In considering the relationship of the blood and hepatic bile cholesterol concentrations, it should be borne in mind that while the cholesterol in the blood is found in both the free and combined states, the bile under normal conditions contains only free cholesterol. It was possible, therefore, that a relationship may have existed between the free cholesterol of the blood and that of the bile. In four experiments in which the free and combined cholesterol of the blood, and the free cholesterol of the bile were determined, we found no evidence of such a relationship.

SUMMARY

1. When dogs were given large doses of desiccated thyroid by mouth or large doses of thyroxin intravenously, there was no demonstrable effect on the cholesterol concentration, or the total cholesterol output of the hepatic bile, although the blood cholesterol fell as low as 40 mg. per cent.

2. When total thyroidectomy was done on dogs there was no demonstrable effect on the cholesterol concentration or the total cholesterol output of the hepatic bile, although the blood cholesterol rose as high as 363 mg. per cent.

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ETIOLOGICAL FACTORS IN ACUTE APPENDICITIS

Based Upon a Study of 3,400 Cases

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FIFTY-TWO years have now passed since the pathologist Reginald Fitz[7] firmly established appendicitis as a definite clinical entity. Since then one would naturally assume that the morbidity and the mortality of appendicitis would have markedly decreased. However, the opposite status has been the strange result here in the United States.

Today the incidence of appendicitis is approximately fifteen times that recorded for the year 1885.[3] The mortality of acute appendicitis has increased 34 per cent in the last quarter of a century. Thus, despite the remarkable advances made in other fields of both medicine and surgery, appendicitis has remained unconquered and its ravages are largely unchecked. It is estimated that now 20,000 persons[1] die from this disease yearly in the United States. When this high death rate is compared to the markedly lowered incidence of appendicitis existent elsewhere throughout the world, it is apparent that continued study on this problem is necessary, in an effort to halt this needless waste of valuable young human life.

The recent contributions of Nicholson,[9] Wangensteen and Bowers,[12] Wangensteen, Buirge, Dennis, and Ritchie,[13] Bowen,[3] Spencer,[11] Wood,[14] Archibald,[2] Robertson,[10] Brown,[6] Bower, Burns, and Mengle,[4, 5] and Nicholls[8] have been of great importance in presenting a clearer conception of the many features of appendicitis. We have been interested, for some time, in the problem of the etiology of acute appendicitis. Recently, our cases have been reviewed from this viewpoint; 3,400 cases of proved acute appendicitis have been studied. The report of the surgeon concerning his operative findings, the pathologist's study of the specimen, and the patient's history were carefully reviewed for data in reference to etiological factors in the causation of that particular instance of acute appendicitis.

There were 2,011 males (59.1234 per cent). The average age of this series was 23.48 years. The aggregate uncorrected mortality was 3.5574 per cent, or 121 deaths. This series was divided into the three following classifications, as recently used by Wangensteen:[12] acute suppurative appendicitis, 1,901 instances (55.8894 per cent); nonperforative gan-

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TABLE I

TABULATION OF THE DEATHS IN THIS SERIES

DEATHS (121 CASES)	ACUTE SUPPURATIVE APPENDICITIS (1,901 CASES)	NONPERFORATIVE GANGRENOUS APPENDICITIS (1,108 CASES)	PERFORATIVE GANGRENOUS APPENDICITIS (391 CASES)
Number	17	51	53
Percentage of 3,400 cases	0.4998	1.4994	1.5582
Percentage of all deaths	14.0488	42.1464	43.7992
Percentage of cases in each group	0.89403	4.60275	13.5521
Sex: Males	12	38	33
Females	5	13	20
Average age of those dying, in years	20.94	23.03	29.16

grenous appendicitis, 1,108 examples (32.5752 per cent); and perforative gangrenous appendicitis, 391 patients (11.4954 per cent).

A study of Tables I and II shows that fecaliths and appendicoliths appear to play a major role in the etiology of both the uncomplicated gangrenous and perforative types of appendicitis. Lymphoid hyperplasia, stenosis, and kinks in the lumen are likewise important etiological factors. Evidence derived from this study showed that appendicitis resulting from enterogenous infection was not uncommon. Foreign bodies and parasites in the appendiceal lumen assumed little significance in this group of cases. The hematogenous origin of acute appendicitis was likewise of minor importance. The etiology of 55.43 per cent of the instances of acute suppurative appendicitis has remained undetermined. The same statement is true concerning 34.81 per cent of all the cases in this entire series.

SUMMARY

The etiological factors in 3,400 consecutive unselected instances of proved acute appendicitis have been briefly indicated. This study demonstrated that fecaliths and concretions in the lumen are the most common etiological factors (30.2326 per cent) of severe acute appendicitis; 20.6388 per cent of this series showed either hypertrophy of the lymphoid follicles, stenosis, or kinks of the appendiceal lumen. These also acted as definite obstructive lesions; 10.4546 per cent of the entire series were believed derived from an enterogenous origin; 1.4582 per cent of the appendices contained foreign bodies in the lumen. Obstructive factors in 50.8714 per cent of this series of acute appendicitis were considered primarily responsible for the acute inflammation. Foreign bodies and parasites in the lumen constituted an additional 2.5520 per cent of this entire group. Obstruction of the appendiceal lumen was responsible for 81.2240 per cent of the examples of acute gangrenous appendicitis, while the same factor caused 79.6341 per cent of the instances of perforative gangrenous appendicitis.

TABLE II

ETIOLOGICAL FACTORS IN THE CAUSATION OF ACUTE APPENDICITIS

(NUMBER AND PERCENTAGE OF EACH TYPE)

	LUMEN FECALITH AND APPENDICOLITHS	HYPERTROPHY OF LYMPHOID FOLLICLES, STENOSES, AND KINKS IN LUMEN	FOREIGN BODIES IN THE LUMEN	PARASITES IN THE LUMEN	ENTEROGENOUS ORIGIN	HEMATOGENOUS ORIGIN	CAUSE IS UNKNOWN
Acute suppurative appendicitis (1,901 Cases)	172 9.04548%	346 18.20614%	39 2.05101%	14 0.7362%	249 13.0949%	27 1.4199%	1,054 55.42986%
Nonperforative gangrenous appendicitis (1,108 Cases)	653 58.93225%	247 22.29175%	11 0.99275%	8 0.7220%	103 9.2957%	12 1.0830%	74 6.67850%
Perforative gangrenous appendicitis (391 Cases)	204 52.1628%	109 27.4713%	3 0.7671%	5 1.2785%	7 1.7899%	7 1.7899%	56 14.3192%
Total cases	1,029	702	53	27	359	46	1,184
Percentage of 3,400 Cases	30.2326	20.6388	1.4582	0.7938	10.4546	1.3524	34.8096

CONCLUSIONS

1. Obstructive factors assume the major rôle in the causation of acute appendicitis.

2. Appendiceal fecaliths and concretions are the most common acute obstructing agent encountered in the two subgroups of this series where 85.9456 per cent of the deaths occurred.

3. The clinical recognition of these obstructing factors will promote better treatment in acute appendicitis.

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CIRCUMCISION

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CIRCUMCISION is a procedure of great antiquity. It has been associated with religious or hygienic rites of many ancient races. While historic reviews are of great interest, the indications for circumcision have changed little during the years.

From a purely urologic viewpoint, we are concerned with the question of infections and obstructions as engendered by a phimosis or a redundant foreskin. In addition to the conditions mentioned above, we have the relationship of phimosis to penile cancer. Wolbarst and Dean agree that there are no recorded cases of epithelioma of the glans penis occurring in a person circumcised in infancy. Dean states the prophylaxis of cancer of the penis is circumcision of all male infants shortly after birth.

The literature is replete with descriptions and comments on circumcision and devices for performing it. Borey, in 1907, presented a very ingenious phimosis clamp. Lewis, in 1914, described a device for this operation, which, differing somewhat in design, was based on similar principles.

In a previous communication (1935) a preliminary report was made of a technique for circumcision in the adult. Since the presentation of 10 cases two years ago, 51 additional personal patients have been operated upon and data obtained by questionnaire on 102 more. The method has been so satisfactory in our hands that a survey of the technique at this time seems warranted.

It is a simple operative procedure which can be readily carried out in the office. The following items are necessary: procaine 2 per cent (with vasoconstrictor), 27 gauge needle, 4 small hemostats, scissors, knife, probe, thumb forceps, needle holder, a piece of No. 25 gauge annealed copper wire, No. 00 plain catgut suture with atraumatic needle, and a proper size circumcision clamp. The clamp consists of 4 parts (Fig. 1): a cone (Fig. 1*a*), a base plate, a top plate, and a screw. The method of its application is described below.

The action of the clamp (Fig. 1*d*) is dependent upon pressure being exercised upon a very narrow rim of tissue which insures adherence of the outer skin and the inner preputial surface. With that accomplished, it permits removal of the redundant tissue and temporarily prevents retraction of the blood vessels. It is, of course, necessary to have a cone which properly fits the glans. This can be determined by a trial fitting

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prior to the procedure. In the personal cases cited above, 6 required a clamp with the base diameter of 3.2 cm.; 52, with a diameter of 2.9 cm.; and 4, with a diameter of 2.6 cm.

With the patient on the examining table, the penis is prepared and draped in the usual manner. Hertzler's method of local anesthesia has been found the most satisfactory. Usually 3 to 5 c.c. of procaine are sufficient for the operation. A circular subcutaneous injection is made about midshaft (Fig. 2*a*); 1.5 to 2.5 c.c. are adequate. Following this, the fore-

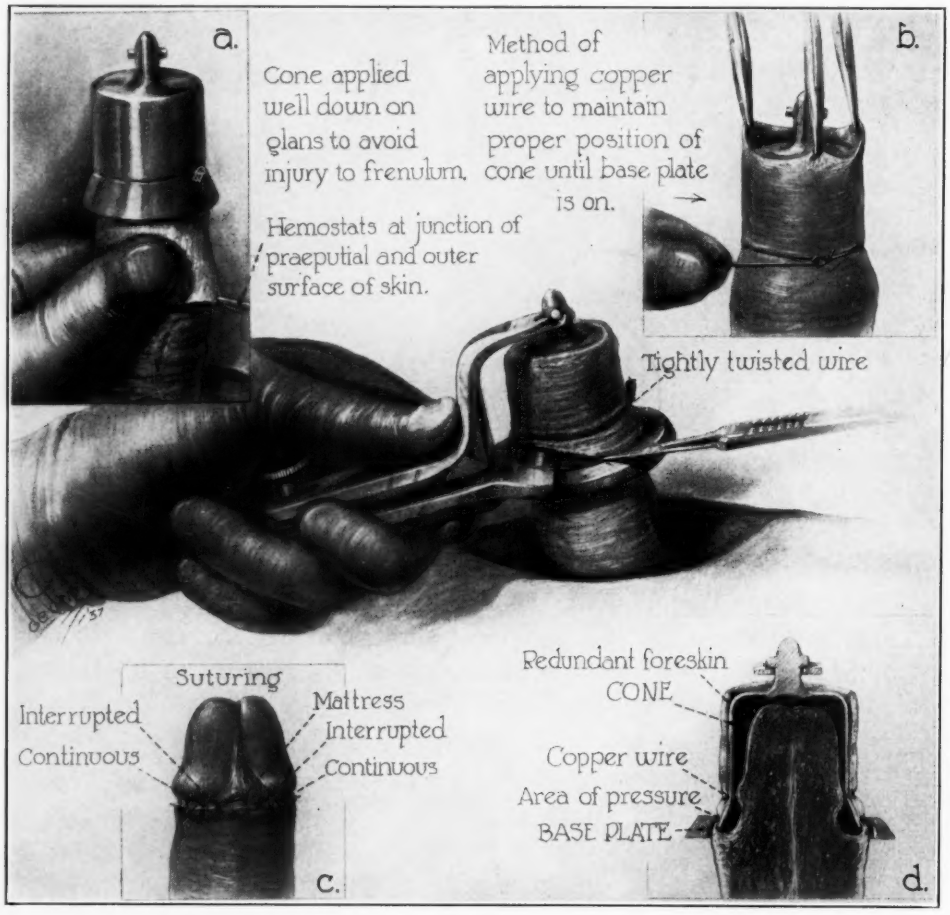

Fig. 1.

skin is retracted and a series of injections are made about the corona. The solution is forced toward the base of the glans (Fig. 2*b*). Considerable care should be exercised to prevent distortion of the tissue. The anesthetic ring must completely encircle the glans and the frenulum should be also infiltrated. Usually 1.5 to 2.5 c.c. are ample.

If the foreskin is not retractible, a line of infiltration is made dorsally and a slit, just long enough to allow complete retraction, is made; then the coronal infiltration described above may be done. All adhesions are

freed. The redundant tissue is grasped by hemostats at the junction of the skin and mucosa and then retracted. The cone, which has been lubricated on its inner surface with a little vaseline, is slipped over the glans (Fig. 1*a*). The mass of tissue is then pulled over the cone. Tension on the hemostats and counter pressure on the cone permit almost any amount of tissue to be removed. However, care in applying the cone is necessary since this prevents any injury to the frenulum. Next, a piece of copper wire is twisted about the redundant tissue to maintain its relationship to the cone (Fig. 1*b*). The hemostats are removed and the base plate is slipped over this mass. The top plate is then hooked under the arms of the cone and slipped into its notch in the base plate and the screw is turned down until it is tight.

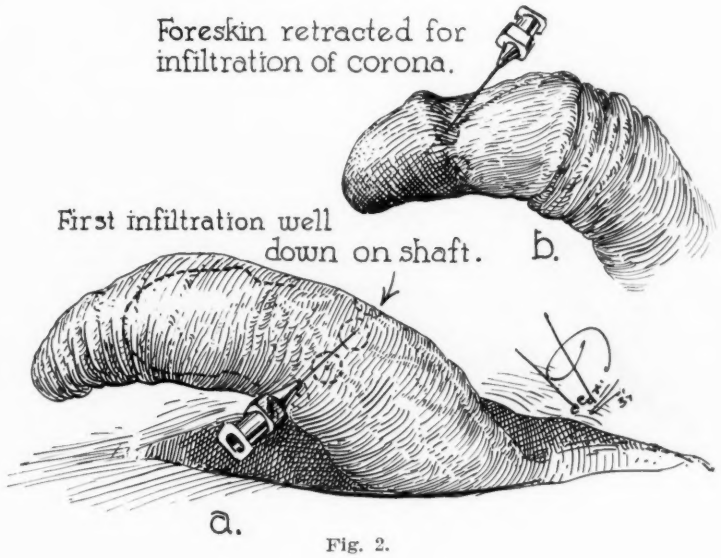

Fig. 2.

At the end of five minutes, the redundant tissue is removed by holding the knife parallel to the base plate and cutting about its circumference (Fig. 1*e*). The instrument is then loosened and removed. This pressure has given temporary coaptation of the cut edges and hemostasis. Since neither of these is permanent, considerable care is necessary in suturing. The first step is a mattress at the frenulum (Fig. 1*c*). Next, two interrupted sutures are placed on either side of this, to complete and maintain the triangle at the frenulum; then a mattress suture is placed dorsally. A simple running suture on either side with rather closely placed stitches completes the procedure.

COMMENT

It is evident that considerable care should be exercised in suturing; any large vessels that can be seen should have a mattress suture placed about them. With care in this step, the operation is practically bloodless.

The sutures usually drop out on the fifth day and the wound is sealed in a week. Simple daily dressings are done. No unusual complications or sequelae have been observed or reported.

NOTES ON INFANT CIRCUMCISION

The technique for infant circumcision was devised by Yellen, who reported 500 cases. I have been able to collect records on 300 additional infant circumcisions. There were no complications noted in this series of 800 cases.

The method is essentially the same as in the adult. There are a few precautions which must be carefully noted.

All adhesions must be dissected free before applying the clamp. Ordinarily, stretching of the prepuce will permit retraction for the dissection; if it does not, a dorsal slit is done. The slit should not be too long, however, since difficulty in keeping the cone in place will be encountered with a deep slit. Only a clamp of the proper size should be used.

No sutures or anesthesia are required in the newborn. In older children a few interrupted sutures suffice.

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Editorial

The Dressing of Infected Wounds

THOSE of us making regular rounds in the wards of large municipal hospitals are struck with the variety of means and methods of the dressing of infected wounds by our resident staff officers. This striking difference in technique employed reflects not only the teaching they have been exposed to but their desire to try various recommended methods. These vary from irrigations and application of various solutions, often highly colored, to adhesive strips neatly latticed across the granulation tissue. The results of the treatment are frequently as varied as the methods.

In 1917 it was my very good fortune to be assigned for a short time to the Rockefeller Institute for a course given for the study of the use of Dakin's solution. One of the outstanding impressions of the course was the meticulous care in which infected wounds were prepared before the treatment by Dakin's solution. The skin was carefully shaved for a distance of three inches around the wound. By the use of sterile soap and water on sterile sponges held on sterile instruments, the skin was gently but carefully and thoroughly washed so that dried pus, blood, scales of skin, or other foreign material was entirely removed from the environment of the wound. This was called the mechanical treatment of the wound.

In 1918 and 1919 in France, almost all of the hospitals were swamped with work and we found ours no exception, so that the time-consuming details of the use of Dakin's solution were confined to a few wards. In the remaining major portion of the wards we decided to use the so-called mechanical treatment of infected wounds. Food carts were converted into dressing carts on which were carried sterile instruments, sterile soap and water, and sterile sponges, in addition to the other necessities. The dressings were lifted off the wound by instruments. Several light scrubbings with small sponges soaked in sterile soap solution followed. Scabs, scales, pus, and blood disappeared, and a sterile dressing was applied without touching the wound with the fingers. The net result of this treatment showed the same improvement in the appearance of the granulation tissue as in the wounds in which Dakin's solution was also used; just as many delayed closures were possible and just as many wounds became as quickly suitable for skin grafting.

Since the War this same technique has been used in our ward at the Cook County Hospital with great satisfaction. The principles are obvi-

ous and the materials are cheap. If the skin surrounding an infected wound is treated as if it were potentially a sterile field, the wound itself is spared contamination by shifting dressings. The granulation tissue contains most of the fighting forces of the body against infection. Left to its own devices and protected from constant recontamination, it soon demonstrates its ability to combat the infection upon it. The result is a wound covered with a red, healthy bed of granulation tissue, with all evidences of healing.

We believe it should be constantly pointed out to our resident staff that the applications of strong antiseptic solutions on granulation tissue have no power to penetrate the granulation tissue to reach infectious bacteria without at the same time injuring or destroying granulation tissue, which after all is the white hope in wound healing.

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Chicago, Ill.

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

REGIONAL ENTERITIS

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BENIGN or nonspecific enteritis or ileitis, localized chronic cicatrizing enteritis, infectious or nonspecific granuloma of the ileum, regional ileitis or enteritis are terms variously applied to the clinical entity, terminal ileitis, first described as such by Crohn, Ginzburg, and Oppenheimer[1] in 1932. Regional enteritis is now favored as the more inclusive term in view of the broadening interpretation of this disease.

The present concept of regional enteritis differs from that of terminal ileitis as described by Crohn and his co-workers[1, 2] only in the magnitude of the intestinal involvement. In their original paper, the disease was described as a benign, subacute or chronic necrotizing and cicatrizing inflammation of unknown origin attacking only the terminal portion of ileum and usually appearing among young adults. The reaction in the ileum results in ulceration of the mucosa, fibrotic invasion and hypertrophy of the muscularis and mesentery which frequently progresses to stenosis of the intestinal lumen and to the formation of multiple fistulas and adhesions. That portions of the small intestine proximal to the terminal part of the ileum might be affected by an identical process was substantiated in 1933 by Harris, Bell, and Brunn[3] who reported a case in which the jejunum was diseased. The following year Brown, Bargen, and Weber[4] observed that the colon adjacent to the involved terminal portion of ileum could be invaded by extension of the process to segments distal to the ileocecal valve. Since 1934, many authors have reported this same finding. Crohn himself favored the view in a more recent report.[5]

Since early in the nineteenth century, references[6-8] have appeared in the literature which attest the recognition of a benign lesion in the small intestine producing stricture, obstruction, abscess, and fistula. These cases were overlooked, except that they were classified with that ill-defined group designated "granuloma of the intestine" which included all benign tumors and did not exclude the specific granulomas caused by tuberculosis, syphilis, and so forth; in fact, many of the lesions were

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considered tuberculous. Braun[9] reported an inflammatory tumor of the sigmoid flexure in 1908. Tietze,[10] in 1920, thoroughly reviewed the literature on benign granuloma up to that time. Moschcowitz and Wilensky,[11] in 1923, reported 4 cases, in 3 of which the colon was involved and in 1 of which the terminal ileum was attacked. In 1931, Mock[12] presented a very comprehensive article dealing with all types of nonspecific inflammatory tumors, principally of the colon, and he definitely established the fact that the specific granulomatous lesions of tuberculosis, syphilis, pathogenic fungi, parasites, and lymphosarcoma were not to be included in the classification. However, the introduction of new concepts regarding regional ileitis and its designation as a distinct clinical entity was the accomplishment of Crohn and his coworkers. Since their report in 1932, more than 100 articles have been published representing reports of more than 500 cases. In a recent survey, Lick[13] reviewed all of the literature in a very comprehensive manner. Certainly the disease is receiving greater recognition than formerly although the question of an increase in its incidence is still debatable. From January, 1922, to September, 1936, 39 proved cases of regional enteritis were encountered at the Mayo Clinic[14] and in the next two years 44 patients have submitted to operation for the same condition. The data used in this paper are derived from the study of these 44 cases.

Very little has been learned about the disease since the time when the first case was reported. Its etiology remains unknown and the ideal form of treatment is yet to be established. Recording of additional cases is useful pending development of a specific plan of treatment.

ETIOLOGY

Numerous observers have suggested possibilities as to the cause of this inflammatory involvement of the intestine, but careful perusal of their studies and even intensive investigation leads one to the conclusion that the etiology remains a matter of conjecture. All patients who come to the Mayo Clinic and who have regional enteritis are subjected to the following investigations preoperatively: (1) The stools are examined for Bargen's diplostreptococcus, for the bacteria which produce dysentery, for *Mycobacterium tuberculosis,* ova, parasites, amoebae, blood, and pus. (2) The blood is tested for the presence of syphilis and for evidence of the various dyscrasias and agglutination tests are conducted against the groups of intestinal bacteria, undulant fever, and tularemia. (3) Intradermal tests for tuberculosis (Mantoux) and lymphopathia venereum (Frei) are performed. (4) Roentgenologic studies of the thorax are made to eliminate the possibility that tuberculosis is present. (5) If fecal fistula is present, the pus and scrapings of the tissue are investigated for evidence of actinomycosis, blastomycosis, and tuberculosis. Postoperatively, extensive bacteriologic and pathologic studies are made of the bowel, mesentery, and lymph nodes. In the last twenty cases

studied at the clinic, Pumphrey[15] has followed every clew or suggestion of other authors and of the bacteriologic department of the clinic, but he was not successful in discovering the etiologic factor in this disease. His findings have been published elsewhere.

None of the aforementioned possible factors accompanied regional enteritis frequently and in those instances in which there was such an association it seemed coincidental.

Felsen[16] is the only one who unequivocally stated that *Bacillus dysenteriae* is the etiologic factor. Mixter[17] reported isolation of an anaerobic streptococcus from a macerated mesenteric lymph node removed from one of his patients. He also suggested the possibility of a racial predilection because of the high percentage of Jews in one reported series of cases.

Jackson[18] held the view expressed previously by Bargen and Dixon[19] that there is a relationship between mesenteric lymphadenitis and terminal ileitis and that both lesions are due to disease of the lymphatic system in the region involved. Probstein and Gruenfeld[20] likewise felt that the lymphatic vessels in the affected site are in some way responsible and these authors expressed the view that stagnation and great abundance of lymphatic tissue in the region account for the frequency of attacks on the terminal portion of ileum. Certain it is that when the bacterial flora of the fecal current reaches the ileocecal valve, it has acquired its maximal degree of infectiousness and toxicity.[21] The experimental work of Reichert and Mathes[22] is of interest concerning this point. They injected irritating and sclerosing materials into the mesenteric and subserous lymphatic vessels and this brought about chronic lymphedema of the intestinal wall. They believed that infection of low grade and concomitant chronic lymphedema are the two dominant features.

W. J. Mayo[23] in a personal communication to the authors suggested the possibility of some acid-fast variant being responsible. He recalled encountering conditions early in his career like those described in modern literature under the term "regional enteritis." At that same time there were many cases of scrofula and tuberculous peritonitis. With the elimination of the source of avian and bovine tuberculosis, all of these entities became rare. In this connection it is to be remembered that in instances of Johne's disease of cattle the small intestine is involved in a process similar to that of regional enteritis and a pseudotubercle bacillus is the etiologic agent.[24, 25] Felsen and Pumphrey are now conducting investigations which should settle this question definitely.

Although the hypothesis that some allergic phenomena are responsible has been advocated, most investigators feel positive that the origin of this disease is bacterial. Its close resemblance to lymphogranuloma inguinale, both in the stage of early involvement of the regional lymph

nodes and in the subsequent stage of severe cicatricial stenosis of the affected portion of bowel would suggest the same type of causative agent; that is, a filtrable virus.

PATHOLOGIC MANIFESTATIONS

The gross and microscopic appearance of the specimens obtained at resection showed the process to be that generally attributed to inflammatory invasion. However, since the disease is of progressive nature, the exact findings depend on the phase in which the operation is performed. Generally speaking, the patients observed at the clinic are in the advanced stages of the disease and the pathologic process has produced unmistakable gross deformity resulting from fibrotic repair after chronic inflammation on which acute exacerbations of the disease have been superimposed. The early phases of the disease are not yet sufficiently well known to prevent the performance of simple appendectomy when resection or a side-tracking procedure would be the more suitable operation.

Descriptions of the pathologic process show striking uniformity. Although the terminal portion of ileum is the segment most frequently involved, no part of the intestinal tract is exempt (Table I). In 20 of

TABLE I

REGIONAL ENTERITIS: SITE OF PATHOLOGIC PROCESS IN 44 CASES

SITUATION	NUMBER OF CASES
Ileum	20
Jejunum and ileum	1
Jejunum, ileum, and cecum	1
Ileum and cecum	14
Cecum	1
Ileum, cecum, and ascending colon	2
Ileum, cecum, ascending and transverse colon	2
Ileum, cecum, ascending, transverse, and descending colon	2
Ileum, cecum, transverse colon, and sigmoid flexure	1

the 44 cases in this series the ileum alone was affected. The jejunum was not attacked solely in any of the cases, but in 1 instance the jejunum and ileum were involved and in another the jejunum, ileum, and cecum were invaded. The ileum and cecum were the site of the disease in 14 cases (Fig. 1); the ileum, cecum, and ascending portion of the colon, in 2; the ileum and the ascending, transverse, and descending portions of the colon, in 2; and the ileum and the ascending and transverse portions of the colon and sigmoid flexure, in 1. The process was confined to the cecum in 1 case.

If an external fistula was present, it was almost invariably the result of an operation in which the diseased portion of bowel was incompletely removed. Internal fistula develops after chronic perforation has occurred The latter process takes place so slowly that it permits segregation of contaminating materials from the general peritoneal cavity, or, at the

most, the formation of a small, walled-off abscess which sometimes discharges its contents into an adjacent viscus. For instance, the terminal part of the ileum may be found to communicate with the bladder, as in a case in which small sinuses led to these organs from a thick-walled abscess having a capacity of about 2 ounces. In addition, fistulous communications between the diseased portion of bowel and the abdominal parietes were present in 8 cases. Intraintestinal communications were present in an equal number of cases, but did not produce symptoms. These small tracts connected a coil of involved ileum and an adherent segment of adjacent bowel, usually the ascending portion of colon, the ileum, or the sigmoid flexure. In 3 instances in this series the sigmoid flexure was perforated.

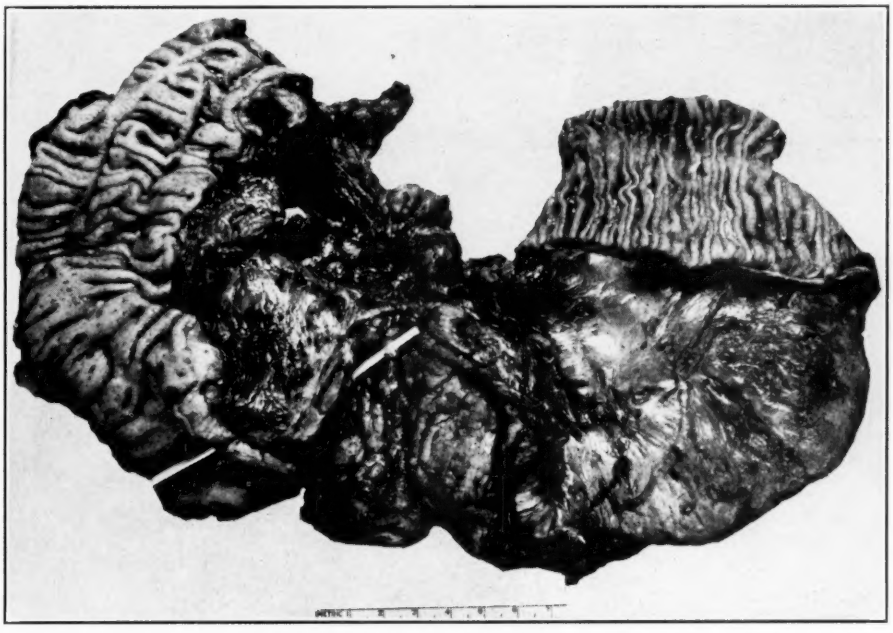

Fig. 1.—Regional enteritis involving terminal portion of the ileum and the cecum, showing the severe hyperplastic type of inflammatory process.

The distal portion of the ileum appeared to be the original site of invasion of the disease in practically all cases. The affected segment is readily discovered on opening the abdomen. According to our observations the most striking gross features are the typical enlargement and loss of flexibility of the affected segment of bowel and the shortened and greatly thickened mesentery in which the regional lymph nodes are large and firm. The tissues have a dusky, bluish-red appearance and a phlegmonous exudate is distributed sparingly over the serosal covering of the intestine.

If obstruction is pronounced, the portion of intestine just proximal to the site of the disease may be extremely dilated and the muscular elements may be hypertrophic. In the instances in which the condition

is of long standing, many exacerbations have occurred and there is evidence of chronic perforation; the terminal ileum and cecum may be bound together in the right iliac fossa, forming a large phlegmonous mass which almost requires chiseling to separate it from the iliac bone and parietal peritoneum. Lying between diseased portions of the intestine there may be segments which are apparently normal.

When the resected specimen is examined, it will be found that the caliber of the lumen of the diseased portion of bowel is greatly reduced due to thickening of the intestinal wall. This loss of elasticity produces

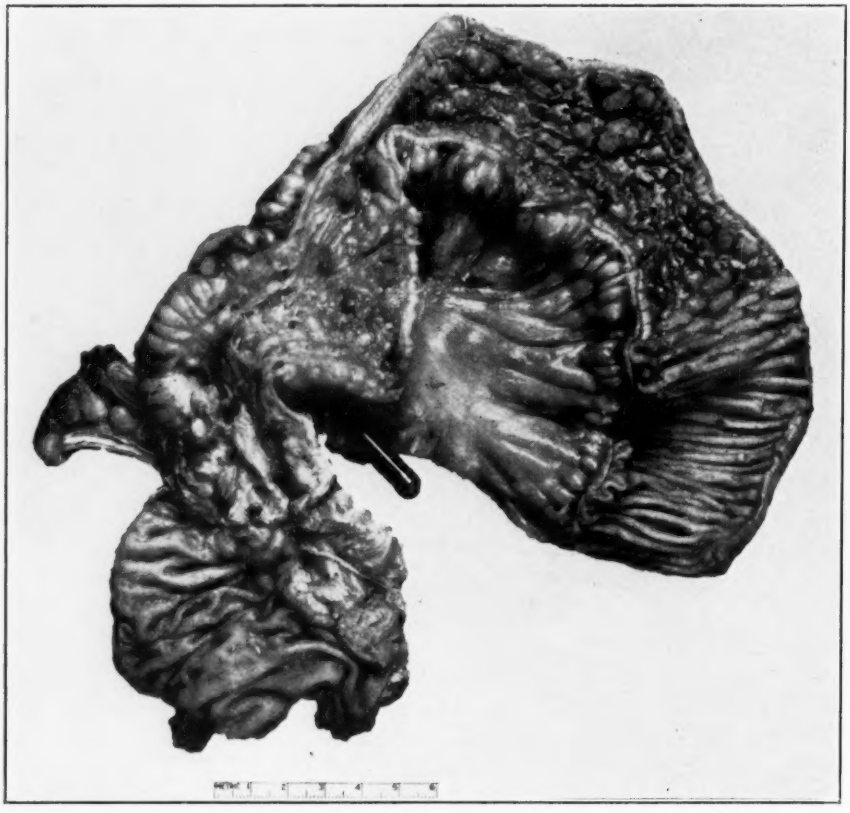

Fig. 2.—Ulceration and destruction of mucous membrane of terminal portion of ileum (from same case as that shown in Fig. 4).

a soggy consistency and hoselike appearance. The mucosa presents a picture varying from that of edema with mild ulcerated regions to almost complete loss of all epithelial structure (Fig. 2). In the typical case the ulcers are found along the mesenteric border and old scars also will be present immediately adjacent to the new regions of ulceration. The intervening mucosa occasionally assumes a pseudopolypoid form. If the terminal portion of ileum is involved, the most advanced pathologic process is generally in the most distal region. The ileocecal valve often will be found entirely obliterated, its lumen being reduced to a

diameter of only a few millimeters by the piling up of fibrotic tissue (Fig. 3). The submucosa and muscularis are greatly thickened, their normal structure being largely replaced by fibrous connective tissue and inflammatory exudate (Fig. 4). The mesentery is very friable and bleeding occurs readily. Furthermore, it is so extensively invaded by

Fig. 3.—Regional enteritis involving the terminal portion of the ileum and the ileocecal valve, with almost complete obstruction at the valve (from same case as shown in Figs. 5 and 6).

the inflammatory process that the attached portion of intestine is likely to be immovable.

Microscopic studies fail to reveal specific characteristics. Evidence of any relationship to tuberculosis, syphilis, actinomycosis, Hodgkin's disease, lymphosarcoma, or other malignant process is not demonstrable. The findings are those of acute, subacute, or chronic hypertrophic exuda-

tive and necrotizing inflammation with proliferative or reparative elements (Fig. 5). The cells of the lymphoid series appear to predominate except in the early acute stages. In the usual chronic process, the small lymphocyte, plasma cell, and fibroblastic elements are in ascendency; eosinophiles occasionally are present. Submucous lymphoid follicles are invariably numerous and are enlarged. Giant cells are encountered frequently, but this is by no means a uniform finding. These large multinucleated cells often contain particles of a crystalline or lipoid nature which have been accounted for as particles of remnants of food that lodged in the ulcerated mucosa. Focal collections of lymphocytes under

Fig. 4.—Greatly thickened mesentery with enlarged inflammatory nodes. Also narrowing and thickening of intestine (from same case as shown in Fig. 2).

the serosa form tubercle-like irregularities which, with the giant cells, undoubtedly account for the erroneous diagnosis of tuberculosis so frequently made in the past.

In the study of twenty-three operative specimens, Coffey[26] found true tubercles with epithelial reaction, central caseation, and typical giant cells in only three specimens. Roentgenograms of the thorax in these three cases revealed the presence of active tuberculosis and the tubercle bacillus was also isolated from the sputum. In no case in this series were the results of roentgenologic examination of the pulmonary fields positive. Acid-fast staining of the pathologic sections did not reveal the presence of *Mycobacterium tuberculosis* and other bacteria were not

encountered with any appreciable degree of uniformity. In cases in which the appendix could be observed, involvement consisted in periappendiceal inflammation which was the result of contiguity, a secondary rather than a primary factor.

CLINICAL COURSE

A clinical entity of pathologic origin as described of necessity would vary considerably in its manifestations, depending on the extent and situation of the involved segment of bowel. Generally speaking, there

Fig. 5.—Microscopic appearance of specimen taken from ileocecal valve. (From same case as shown in Figs. 3 and 6.)

are four phases through which the disease may pass. The earliest manifestation is that of an acute inflammatory lesion. As the terminal portion of the ileum is the most frequent initial site of the disease, the irritation of this portion of intestine and its adjacent peritoneum produces a picture difficult to distinguish from acute appendicitis. The most frequent symptoms are fever of low grade, leucocytosis, nausea, vomiting, epigastric or right lower quadrant tenderness and pain. Diarrhea and cramps are unusual at this stage of the process. That such symptoms are confusing is attested by the fact that twenty-four of our forty-four patients were subjected to appendectomy prior to coming for treatment

in one of the later phases of regional enteritis. As the disease advances, intermittent attacks of diarrhea are characteristic. This is the stage most frequently confused with chronic ulcerative colitis. The typical syndrome of enteritis of low grade prevails; the patient has fever, anemia, a palpable mass in the right lower abdominal quadrant, and has lost weight; his stools are loose or watery and if any pain is present it is mild and colicky.

Remission of symptoms is frequent in the two stages described, but as the stenosing effect of the disease increases the periods of relief are of shorter duration than before and are less common. The symptoms typical of intestinal obstruction are superimposed on those of chronic enteritis. The attacks of diarrhea are more profound and are accompanied by severe abdominal cramps, borborygmus, abdominal distention, or visible contracture of the coils of the small intestine proximal to the involved segment. Malnutrition and anemia become prominent features since much nourishment and fluids are lost because of the diarrhea; furthermore, intake of food and fluid may be greatly limited on account of persistent nausea or even vomiting.

The fourth and final phase of the disease is attained either when acute obstruction is superimposed on the chronic condition or when perforation of the bowel occurs and formation of an abscess or fistula ensues. As stated previously, the fistula may communicate with an adjacent portion of the intestine or with other viscera or with the abdominal parietes. The debility occasioned by the sepsis and decrease in absorption of nutritional elements and of fluids assumes great significance and in itself may be the important factor in a fatal termination.

The course of regional enteritis as delineated is uniform only in a very general way. In the individual case the first signal of impending trouble may be the onset of the syndrome of the late phases, or the symptomatology may have progressed from that of an occasional episode of pain in the right lower abdominal quadrant or in the epigastrium to that of intestinal occlusion although there has been very little intervening disturbance. In an occasional case, the chief complaint will be one which is only remotely associated with the malady. An instance is recalled in which the terminal part of the ileum was found to be the nidus for infectious arthritis. In another case, peptic ulcer was thought to be responsible for the preprandial pain and profound anemia caused by melena until inflammation and ulceration of the terminal portion of ileum were found through roentgenologic studies.

CLINICAL FEATURES

The ages of the 44 patients reported on in this review ranged from 12 to 54 years at the time of onset of the symptoms, although 63 per cent were less than 30 years of age and 84 per cent were less than 40 years of age at the onset of the illness (Tables II and III). The aver-

TABLE II

REGIONAL ENTERITIS: AGES AND DURATION OF SYMPTOMS IN 44 CASES

Average age at onset of symptoms	27.3 yr.
Average age when seen at clinic	31.4 yr.
Maximal age at onset of symptoms	54.0 yr.
Minimal age at onset of symptoms	12.0 yr.
Average duration of symptoms before being seen at clinic	4.1 yr.
Shortest duration of symptoms	4.0 days
Longest duration of symptoms	25.0 yr.

TABLE III

REGIONAL ENTERITIS: AGE INCIDENCE IN 44 CASES

AGE, YEARS	NUMBER OF PATIENTS	
	AT ONSET OF SYMPTOMS	ON ARRIVAL AT CLINIC
Less than 20	6	12
20 to 29	16	16
30 to 39	14	9
40 to 49	2	5
50 to 59	6	2

age age at the beginning of symptoms was 27.3 years. The disturbance had been present for about 4 years before the patients were seen in the clinic. The shortest duration of symptoms was 4 days and the longest was 25 years (Table IV). A third of the patients had been sick less

TABLE IV

REGIONAL ENTERITIS: DURATION OF SYMPTOMS IN 44 CASES

	DURATION OF SYMPTOMS, YEARS							
Years	1 or less	2	3	4	5	5 to 10	10 to 15	20 to 25
Cases	15	7	6	4	2	7	2	1

than 1 year and half of the patients less than 2 years. The course of the disease extended over 10 years in only 3 cases. The average age of the 44 patients when seen at the clinic was 31.4 years. Twenty-four of the 44 patients were males; more than 20 per cent were Jews. Other racial predilections were not noted. The disease has not been observed among Negro patients at the Mayo Clinic.

The chief presenting complaints were: (1) pain, which was not of the cramp-like character associated with diarrhea, in 13 cases; (2) diarrhea in 8 cases; (3) diarrhea and severe abdominal cramps in 13; and (4) fecal fistula in 9. One case did not seem to fit into any of these categories as the only manifestation was a palpable mass in the right lower quadrant of the abdomen.

The pain, other than the cramping pain of the obstructive phase, was of two main types. One type was not dissimilar to the distress of peptic ulcer, being situated principally in the epigastrium. It was dull and intermittent in character and usually was precipitated or was exaggerated by eating and was accompanied by gaseous distention. The other

TABLE V

REGIONAL ENTERITIS: FREQUENCY OF SIGNS AND SYMPTOMS IN 44 CASES

SIGN OR SYMPTOM	NUMBER OF CASES
Loss of weight (average loss, 21.9 pounds)	43
Palpable mass (positive roentgenogram)	32
Diarrhea (average number of stools, 3 to 6)	30
Fever	28
Obstruction	28
Abdominal cramps	25
Anemia	18
Nausea and vomiting	18
Pain other than cramps	12
Blood in stool	7
Fecal fistula	9
Arthritis	3
Tarry stools	1
Appendectomy, on account of symptoms	24
Remission of symptoms	28

type of pain generally occurred in the right lower abdominal quadrant in severe episodes of a few minutes to a few hours' duration and was relieved on occasions by catharsis or by nausea and vomiting. These seizures of pain usually were not accompanied by diarrhea or by cramps although three patients reported an attack of diarrhea.

The diarrhea usually was mild and almost always it was less severe than that accompanying chronic ulcerative colitis. The character of the stool varied from mushy to liquid and, on the average, defecation occurred three to six times in twenty-four hours during a period of activity. One patient reported passing twenty stools in twenty-four hours, which was the maximal number. Generally, gross blood was not passed by rectum, although this did occur in seven of the forty-four cases.

There was usually some cramping pain even in the early stages, although it was not severe. After severe cramping pain began to occur with the attacks, there might be alternating periods of diarrhea and constipation. The diarrhea associated with these intense colicky spasms was of a disturbing nature necessitating frequent evacuation of the bowels, often accompanied by tenesmus. The cramping pain was most severe in the right lower quadrant of the abdomen. It was accompanied by or was relieved by the passage of a loose, watery stool containing mucus and much gas and occasionally by nausea and vomiting. A palpable mass in the right lower quadrant of the abdomen, intestinal obstruction, and severe malnutrition were more frequent among the patients who complained chiefly of abdominal cramps and diarrhea.

Nine patients had external fecal fistulas, one of whom passed feces and gas through the urethra. All of the fistulas developed after the performance of inadequate operative maneuvers in the region of the diseased intestine, most frequently after appendectomy. The fistulas extended from the involved portion of ileum or cecum or from both sites to the right or lower middle region of the abdominal wall. In the case in which

the tract formed a communication between the terminal ileum and the bladder, the sinus had no other external outlet. Four of these nine patients also had intraintestinal fistulas. Fecal drainage from the abdominal fistulas in five cases was profuse and generally the skin surrounding the external stoma was excoriated to the extent that it caused much distress.

The frequency of appearance of various signs and symptoms (Table V) in this group of 44 patients was as follows: loss of weight, 43; palpable abdominal mass, 32; diarrhea, 30; fever, 28; obstruction, 28; abdominal cramps, 25; anemia, 18; nausea and vomiting, 18; pain other than cramps, 12; blood in the stools, 7; fecal fistula, 9; arthritis, 3; and tarry stools, 1. Twenty-eight patients had experienced remissions of their symptoms.

Loss of weight was a characteristic feature of the disease. Each patient had experienced some loss of weight, varying from 2 to 60 pounds; the average loss was 22 pounds.

In the typical case the abdominal mass was found in the lower right side of the abdomen. Usually it was situated rather deeply except among those individuals who had lost much weight, in some of whom the mass was visible as well as palpable. In most instances the mass was firm and dense and did not present the nodular hard consistency characteristic of cancer. It was irregular but smooth, only slightly tender, fairly well fixed, and did not cause reflex rigidity of the abdominal muscles. Distention of loops of bowel may be detected mesial to the mass both by palpation and by visible peristalsis. Occasionally, coils of small intestine are matted together below the brim of the pelvis and can only be felt through the vagina or rectum. In such a case, the differential diagnosis must exclude lesions of the pelvic viscera. The first evidence of an intestinal disorder may consist in detection of a lump in the right side of the abdomen or in embarrassment of the patient from excessive rumbling of gas (''growling'').

The blood is practically normal in more than half of the cases. Butt and Watkins[27] have reported the occurrence of a macrocytic anemia in certain instances of terminal ileitis. This anemia did not respond to the administration of the antianemic factor effective in pernicious anemia; however, spontaneous recovery from the anemia occurred following successful extirpation of the diseased segment of bowel. The anemia encountered among eighteen of the patients who had regional ileitis was typically a mild hypochromic anemia, although a severe toxic type of anemia was present in a few cases in which the chief complaint had been severe cramps and diarrhea. The patient whose concentration of hemoglobin was lowest had 9.5 gm. per 100 c.c. of blood; erythrocytes numbered 3,200,000 per cubic millimeter of blood. In the chronic phases of the disease, the number of leucocytes was found to be normal or only

slightly elevated if complications were not present; however, the sedimentation rate of erythrocytes was characteristically increased. The chief features of the other symptoms have been outlined.

ROENTGENOLOGIC EXAMINATION AND MANIFESTATIONS

The barium meal and the barium enema are both used as means of investigating the cecum and terminal portion of ileum and each method has

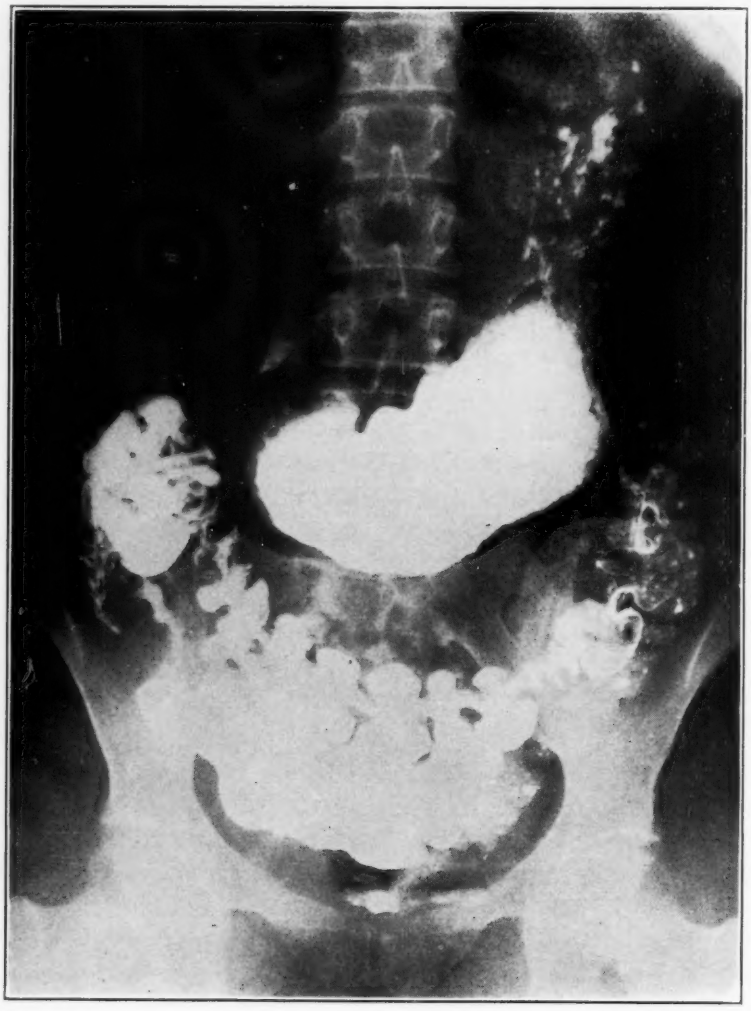

Fig. 6.—After barium meal, showing extreme constriction of lumen of terminal portion of the ileum (from same case as shown in Figs. 3 and 5).

its proponents (Figs. 6 and 7). At the Mayo Clinic, the barium enema is used as the preliminary mode of filling the bowel preparatory to roentgenologic examination. Weber[28, 29] stated that with the contrast enema the coils of the ileum are well elevated out of the pelvis, are distended, and are readily manipulated under roentgenoscopic control by palpation

through the abdominal wall. Furthermore, one must not overlook the danger of filling the proximal part of the intestine with a substance which will pass through the partially obstructed lumen with difficulty. Conversion of partial occlusion into complete obstruction is a conceivable result which may have grave consequences. However, the proximal portion of ileum of necessity must be examined after a contrast meal and

Fig. 7.—After barium enema, showing deformity of cecum and terminal portion of ileum with loss of the mucosal pattern (from same case as shown in Figs. 3 and 5).

therefore the meal is given if a more extensive or confirmatory investigation is desired.

Weber[28, 29] has correlated the roentgenologic manifestations with the presenting pathologic characteristics and has described two general types. His word picture of the conditions found on examination with the contrast media is unsurpassed: "With the hyperplastic character of the

pathologic process in predominance, then the roentgenologic manifestations will be such as are directly or indirectly attributable to hyperplasia. Such changes are narrowing of the lumen due to encroachment on it by the more or less markedly thickened intestinal wall; shortening of the affected segment, due to contraction of the hyperplastic tissue; loss of normal pliability and mobility noted when the diseased intestine is manipulated during the roentgenoscopic examination. With ulcerative features in predominance pathologically, these will be prominent in the roentgenographic picture. Narrowing, shortening and rigidity of the affected segments will not be so manifest, but revealing changes are to be looked for in the pattern of the mucosal relief of the ulcerated segment. Normally, the relief is abundant, but local or general denudation of the internal surface of the intestine is exhibited roentgenologically by a flat, moist, stippled relief which is readily recognized as abnormal. The usual combination is that of hyperplasia and ulceration, with the former predominating. A purely hyperplastic form is only a little more apt to come under observation than a purely ulcerative form. Such complications of this kind of regional enteritis as intra-abdominal and external fistula are demonstrable at roentgenologic examination without great difficulty.''

Kantor[30] listed four chief changes in the ileum: (1) a filling defect just proximal to the cecum, (2) abnormality in contour of the last filled loop of ileum, (3) dilation of loops of ileum just proximal to the lesion, and (4) a ''string sign'' representing the actual lesion.

Thus, the roentgenologic findings are characteristic of the disease. However, they are not pathognomonic because they occur to a certain extent in association with other stenosing lesions of the terminal part of the ileum. The differential roentgenologic diagnosis as regards intestinal neoplasm affords no difficulty with the exception of those lesions which have caused perforation. And even in such cases, careful examination shows the malignant process to be more abruptly demarcated and the mucosal pattern completely eradicated, and on palpation the lesion is hard and knotty owing to induration. Tuberculous enteritis affords the greatest difficulty in diagnosis and it may be a problem for even the most experienced roentgenologist. The general features of both forms of enteritis are much the same. However, Weber[28, 29] has noted that the tuberculous intestine has a rougher and more corrugated appearance than one affected by regional enteritis and the changes correspond to the more irregular development of the ulcerohyperplastic process. Extraintestinal foci of tuberculosis, especially of the lungs, afford the final differential factor. It is conceivable that nonspecific enteritis could occur in the presence of an active tuberculous focus, but we are inclined to classify all such lesions as tuberculous. None of the 44 cases of regional enteritis in this series showed any roentgenologic evidence of pulmonary tuberculosis. The intestinal tract was examined roentgenoscopically in 39 of the cases by use of contrast media. In 5 instances the investigation was omitted

because of the presence of obstruction. The diagnosis of regional enteritis was correct in 36 of the 39 cases. The results of examination of the films in the 3 remaining cases were negative as far as the presence of any such process was concerned.

DIAGNOSIS

If the diagnosis of regional enteritis is to be made before operation is undertaken, the symptom complex must be borne in mind constantly. Even then, in an isolated case, the patient may come to operation without a suspicion as to the true nature of the condition having been expressed. In our series of cases an incorrect diagnosis occurred most frequently among those patients who had not experienced symptoms associated with the gastrointestinal tract. The presenting complaint was pain low in the abdomen and on examination a tender pelvic mass could be palpated in the region of the uterine adnexa. An ovarian or tubal abscess was the logical diagnosis. The real cause of the trouble was only determined at the time of operation.

The features of particular importance in making the diagnosis are: (1) acquaintance with the protean manifestations of the disease; (2) presentation of a history suggestive of the ailment which generally includes a report of previous appendectomy, pain, or cramps that have been especially prominent in the right lower quadrant, bouts of mild diarrhea, loss of weight, and fever of low grade; (3) an examination which reveals a mass in the right lower quadrant of the abdomen or evidence of the formation of fistula, emaciation and anemia, scar of a previous appendectomy, evidence of intestinal obstruction, excessive peristalsis, borborygmus, and abdominal distention; (4) roentgenographic evidence of a stenosing lesion of the cecum or of the terminal portion of ileum; and (5) ruling out of all other lesions which, if present, could produce a similar symptom complex.

The roentgenologic findings are by far the most important element in making a definite deduction; in fact, the diagnosis must be largely a matter of conjecture until the definite deformity of the bowel is visualized by the use of contrast media.

Of the conditions that must be considered as a possibility in attempting to make a differential diagnosis, chronic ulcerative colitis probably takes first place; especially is this important because chronic ulcerative colitis is most effectively treated by medical means; whereas, regional enteritis is a surgical problem. Generally, the distinction can be made readily by the use of the sigmoidoscope and barium enema in conjunction with a consideration of the clinical features. However, the diagnosis is more difficult to make in the 5 to 10 per cent of patients who have chronic ulcerative colitis and among whom the ulcerative process involves the proximal portion of the colon and the rectum is normal. Nevertheless, examination with the aid of the barium enema usually will furnish sufficient information on which to make the distinction.

Other lesions to be considered are the specific granulomas, such as tuberculosis, syphilis, actinomycosis, amebic or parasitic tumors; various types of malignancy, such as scirrhous carcinoma, lymphosarcoma or Hodgkin's disease, and mass-producing lesions of the female adnexa and cecal appendix. It is certain that the malignant processes and the mass-producing lesions cannot be ruled out definitely except by performing an exploratory operation.

If a fecal fistula is present, besides making an investigation for acid-fast bacilli and sulfur granules, one must take into consideration the possibility of a foreign body, appendiceal abscess, or sequelae of a surgical accident being present.

Finally, the diagnosis is achieved when clinical suspicion has been fortified by a suggestive roentgenographic deformity and the elimination of all other etiologic factors to such an extent that laparotomy is deemed justifiable. However, the diagnosis is accomplished with certainty only after the diseased portion of bowel has been resected and examined grossly and microscopically.

In one-fourth of the cases the condition had been diagnosed correctly prior to observation at the clinic. In the remainder of the cases the order of frequency of other diagnoses was as follows: appendicitis, chronic ulcerative colitis, amoebic dysentery, fecal fistula, tumor of the bowel, duodenal ulcer, pelvic tumor, tuberculosis of the cecum, intestinal obstruction, and irritable bowel. Sixty-seven different diagnoses were made in 35 of the cases; in 9 cases a diagnosis had not been made; 40 of the 44 cases were correctly diagnosed at the clinic before surgical intervention.

The presence of three cardinal features is of great aid in reaching a correct diagnosis. In our series a palpable mass was present in 31 cases, chronic obstruction of the small bowel occurred in 28, and positive signs were observed on roentgenologic examination in 36 out of 39 cases. The remaining 5 were not given either the barium meal or the enema as obstruction was nearly complete. Of the 44 cases, only 2 did not have any of these features; 21 exhibited all three features, and in 12 others only one of the three features was lacking. Of 9 cases in which only one feature was present, roentgenographic evidence of the disease was obtained in 6, obstruction was found in 2, and a palpable mass was detected in 1. It is evident that in 95 per cent of the cases some of the three features will be found in combination, and, if the history is suggestive, if the roentgenologic examination of the thorax does not reveal a tuberculous process, if fever of low grade is present and the sedimentation rate is elevated, the clinical diagnosis is assured as nearly as is possible before exploration.

TREATMENT

There is no known medical regimen of value in curing this malady. Spontaneous cures have been recorded by the majority of observers who

have had a wide experience. However, the probability that these individuals may later experience a relapse and that the disease will progress to its later stages is something which can be determined only by the lapse of time. Certain it is that among those individuals who have experienced progression of the disease to the extent that there is ulceration, stenosis, malnutrition, obstruction, fistula, or formation of abscess surgical intervention is the only means of combating the irreparable damage to the intestine.

In 32 of the 44 cases here recorded, a preliminary course of medical treatment had been followed for as long as 4.2 years. In the majority the therapy was symptomatic and was given without knowledge of the underlying pathology, but according to the histories of the whole group of patients almost every conceivable mode of attack in the physicians' armamentarium had been given a trial without allaying the inevitable terminal stage. One patient was observed for a period of seven years and during that time underwent three abdominal operations for other conditions. The progress of the intestinal process was observed on an average of every two years and in the interval between operations a medical regimen was carried out with excellent cooperation between physician and patient. At the end of the seventh year and at the time of the third operation it was observed that obstruction of the terminal portion of ileum had become severe, intraileal fistula between the coiled loops of thickened, soggy intestine had occurred, and the involvement had extended from the original site in the terminal part of the ileum to include almost five feet of the bowel immediately proximal to the original lesion. The patient had lost fifty pounds and was greatly disturbed by severe abdominal cramps and spells of nausea and vomiting and she was decidedly restricted in her activities because of evacuation of her bowels ten to fifteen times daily. It was evident that this patient's condition did not warrant further temporizing and her physician referred her to the clinic for surgical attention. Resection was carried out in one stage, removing all of the involved portion of ileum, the cecum, and ascending colon, with wide extirpation of the mesentery and large mesenteric nodes. The continuity of the bowel was re-established by ileotransverse anastomosis. A more difficult resection could not be imagined as the whole of the terminal segment of ileum and the cecum formed one large, beefy, phlegmonous mass, which was adherent in the right iliac fossa and had to be freed from such retroperitoneal structures as the ureter, ovarian vessels, and iliac vessels. The patient's postoperative course was uncomplicated except that there was some infection of her wound. One year later she reported a gain of thirty pounds, freedom from all discomfort, and a normal state in all respects except a tendency to have loose bowel movements (averaging about four stools daily).

It is difficult to understand how any physician could conscientiously advise such a patient to forego surgical intervention and to continue to

adhere to a regimen that, if carried further, would certainly have had a disastrous result. Anyone who has observed a case such as that described or who has seen the irremediable damage sustained by the affected segment of intestine must realize that there is no known medical treatment that will dissolve the fibrotic stenosis which has replaced the normal elements or that will close the fistula that develops in the later phases of terminal ileitis. However, it is conceivable that a specific remedy may be found eventually that will allay the disease in its early stages or will prevent recurrence of the process after surgical removal of the damaged or fistulous bowel.

Twenty-seven patients had undergone some operation before coming to the Mayo Clinic. These procedures consisted of 24 appendectomies, 6 ileocolostomies, and 4 resections. Exploration or drainage of an abscess brought the total to 41 operative procedures. Sixty-two operations have been performed at the clinic on this same group of patients, bringing the total number of surgical interventions for the 44 individuals to 103.

After surgical intervention has been decided on, much further thought and consideration will be required to determine the exact procedure most suited to the case (Table VI). Should one attempt resection and anasto-

TABLE VI

REGIONAL ENTERITIS: DETAILS OF SURGICAL TREATMENT IN 44 CASES

SURGICAL TECHNIQUE EMPLOYED		INDIVIDUAL FREQUENCIES	SUBTOTALS
Ileocolostomy*	End-to-side	1	14
	Side-to-side. Cut across in 3 cases, not cut across in 10	13	
One-stage resection†	Ileocolostomy and resection of transverse colon, side-to-side	12	14
	Ileocolostomy and resection of ascending colon, end-to-side	1	
	Exteriorization	1	
Two stage resection	Ileocolostomy with transverse colon, side-to-side	12	15
	Ileocolostomy with ascending colon, end-to-side	2	
	Ileo-ileostomy, side-to-side	1	
Exploration	With freeing of adhesions	1	1

*One ileostomy performed.

†Witzel enterostomy also performed at the time of resection in 8 cases.

mosis in one stage, which will save the patient time and expense, or would it be more judicious to approach the problem conservatively by making a simple ileocolostomy as a primary procedure, carrying out a resection only after a period of observation? Curiously, experience has led to the practice of employing the more radical procedure in those cases in which the pathologic process is most advanced and in which, from a theoretic standpoint, the operation is not likely to be tolerated well. The logic of this is readily discernible when one recalls that in the early stages of the disease the process has been known to subside spontaneously. In this

phase, a simple short-circuiting operation carries a very low mortality and provides an opportunity for the diseased segment of bowel to improve by being placed at rest. If the trouble continues to advance subsequently, resection can be undertaken with the advantage of having one stage of the operation completed and of having the organism adjusted to the unnatural fecal pathway.

For those among whom the pathologic process is so far advanced that temporizing has nothing to offer, primary radical extirpation of the diseased segment, if at all feasible, has much in its favor. This is particularly true if only the terminal portion of ileum is involved, or, at the most, the terminal part of the ileum and its adjacent colonic segment. In these instances, there is the choice of performing ileocolostomy with or without division of the ileum and of making a resection at that same time or at a subsequent time. In the advanced stage of the disease, such as was present in the majority of our cases, obstruction, fistula or both have developed and side-to-side ileocolostomy without transection of the ileum would only partially deviate the fecal current, and the cramping pain, reflex nausea and vomiting and even the diarrhea would not be completely relieved. With this situation obtaining, the patient can make very little headway in preparation for the second stage of the operation. Furthermore one is frequently disappointed if it is expected that with the involved segment only partially at rest the infection will subside and will permit resection to be made more easily. If ileocolostomy alone is to be employed, it is true that the fecal current can be side-tracked completely by transecting the ileum proximal to the diseased region and by inverting the distal stump. However, if the obstruction is severe an almost "blind segment" obtains and there is the possibility that a blowout of the closed stump will occur. Also, reflex disturbances and toxic manifestations continue unabated in some of the cases. Extension of the disease has been known to occur between the two stages of the operation with ensuing involvement of the region of anastomosis. Should the disease extend after ileocolostomy, which has been accompanied by transection of the ileum in an uninvolved proximal segment, it would seem highly probable that the spread occurred by way of the diseased mesentery and lymphatic structures which were left in situ.

When ileocolostomy is made to prevent the flow of feces through a fistulous tract, it is evident that the entire fecal current must be side-tracked. Even then, although the feces no longer extrude through the abnormal opening, the origin of the tract in the infected segment of intestine has not been disturbed and will not close. Occasionally, when a large quantity of fluid and unabsorbed elements of food are being lost through an external fistula and there is severe excoriation of the abdominal skin, it would seem logical to precede resection by diversion of the intestinal contents as described. Thus rehabilitation in this way undoubtedly would make the risk of resection less. However, it is unusual

for the fistula accompanying regional enteritis to be that extensive; the debility which is present is generally that occasioned by the presence of the disease rather than by loss of the substances mentioned. For this reason very little is attained by a simple short-circuiting procedure. In the 9 cases of fecal fistula, 18 operations had been performed before the patients came to the clinic and regardless of these procedures the fistula had not been eliminated. The fact is that in each instance the fistula occurred after performance of an operation at which time the diseased bowel was not removed.

What may one expect from resection and anastomosis in one stage when the disease already has progressed to a late phase? It will be found that the patient obtains relief from his discomfort, that extensive progress of the disease toward an uninvolved region is obviated as nearly as possible, that fecal fistulas are eliminated if present, and that the likelihood of occurrence of a fistula postoperatively is extremely remote. Also, the return of the patient to his normal pursuits has been expedited by many months. The only question then is: Does an operation in one stage subject the patient to an unjustifiable and avoidable risk? Observations do not warrant such a conclusion if one considers the results obtained in properly selected cases. Most of the patients who had regional enteritis were in the period of life in which surgical intervention is withstood particularly well. Also, the attending circumstances seem to militate against the likelihood of the occurrence of that most dreaded and very frequent complication of intestinal surgery; that is, peritonitis. The infection in the wall of the intestine has exposed the peritoneal cavity to contamination for such a lengthy period in most cases that considerable immunity to subsequent infection has apparently ensued. Peritonitis was not the cause of death in any case in our series.

Among older patients, in the upper limits for the occurrence of such a process, and particularly among those who have involvement in several regions of the small intestine, the conservative procedure would seem to be a necessity. This is especially true if an abscess has formed. The surgical procedures undertaken on behalf of the patients in our series consisted of 14 side-tracking operations (13 ileocolostomies and 1 ileostomy); 15 resections in two stages, 14 resections in one stage, and 1 exploration with the freeing of adhesions (Table VI).

Of 14 exclusion procedures (ileocolostomies), 13 were effected by side-to-side anastomosis (12 to the transverse colon and 1 to the descending colon); in 1 case the intestines were anastomosed end-to-side. In 3 instances the ileum was divided and the distal stump was inverted. The ileostomy was of the loop type, with both the distal and proximal stomas exteriorized. The postoperative complications in these cases were acute diarrhea, 2 patients; fecal fistula, 1; infected wound, 2; otitis, 1; intestinal obstruction, 1; hemorrhage, 1; and embolism, 1. In the cases in

which embolism, intestinal obstruction, and hemorrhage occurred, death ensued. Severe debility associated with a state of deficiency and pneumonia was responsible for one additional death.

One to two years after surgical treatment, 4 patients were dead, 5 were in good health, 2 were either unimproved or were in a worse condition than before operation, and 3 reported a gain in weight but the latter had been operated on too recently to foretell their ultimate course (Table VII).

TABLE VII

REGIONAL ENTERITIS: RESULTS OF SURGICAL TREATMENT IN 44 CASES (6 MO. TO 2 YR. POSTOPERATIVELY)

STATUS	OPERATION			
	ILEOCOLOSTOMY	ONE-STAGE RESECTION	TWO-STAGE RESECTION	EXPLORATION
Dead	4	1	2	
Good	5	12	12	
Poor	2			
With persistent fistula	3			
Unchanged		1	1	
Not reported				1
Total	14	14	15	1

In several of the cases in which resection in two stages was performed, ileocolostomy had been carried out primarily, but continuation of the symptoms or progress of the disease was responsible for the decision to employ resection. The average time between stages was three months, although in one case resection was carried out within two weeks of the time of ileocolostomy and in another, one year lapsed before the second operation. The type and situation of the anastomosis in the 15 cases is of interest: In 12 instances ileotransverse colostomy was performed and in 2 the ileum was attached to the ascending colon. Twelve of the 14 ileocolostomies were made by lateral anastomosis and 2 were effected by end-to-side union. The ileum was transected and the distal stump inverted in 3 of these cases. In the remaining case, the midileum was involved and side-to-side ileoileostomy was performed and was followed six months later by removal of the segment. The terminal portion of ileum, cecum, ascending colon, and a part of the transverse colon were removed in 10 cases; in 3 the resection embraced the terminal portion of ileum, cecum, and first portion of the ascending colon; in 2, a large segment of the involved midileum alone was extirpated. One patient was subjected to another anastomosis between the ileum and sigmoid two years after the original resection was performed because of a recurrence at the site of the anastomosis and in the transverse colon. The patient died and this was the only surgical death in the group. His death followed development of a fecal fistula, infection of the wound, and general sepsis.

The other postoperative complications among this group of patients were: pneumonia in 2, epididymitis in 1, gastric retention in 3, fecal fistula in 2 (closed spontaneously), and pharyngitis in 1.

What were the results of the two-stage procedure? There were 2 deaths, the one aforementioned and one nine months postoperatively (Table VII). In the latter instance, even at the time of the resection, the process had extended to the transverse colon. Diarrhea had increased in severity and there was an ensuing deficiency syndrome simulating pellagra. Finally, pneumonia was superimposed and death occurred. One of the 13 patients reported being in the same condition as before operation; 12 were well and had gained on the average about fifteen pounds. However, less than six months had lapsed since completion of the surgical treatment of 4 of the latter group and the ultimate results are not yet certain.

Resection in one stage was performed with 13 anastomoses of the ileum to the transverse colon or to the hepatic flexure. Simple exteriorization of the terminal portion of ileum and ascending colon, as a modified Mikulicz procedure, was effected in 1 instance. A side-to-side inosculation was used in all except 1 case in which end-to-side union was made. A Witzel type of catheter enterostomy was provided proximal to the anastomosis in 8 instances.

There were no surgical deaths among patients who had a resection in one stage (Table VII). The complications encountered included abscess in one case, infected wound in 3, ileus in 2, gastric retention in 1, acute dilatation of the stomach in 1, embolism in 1, and pneumonia in 1.

The results of such treatment were as follows: One patient died four months postoperatively from multiple thrombosis of doubtful association with the disease under consideration. Twelve patients reported good results including an increase in weight from ten to thirty pounds. One patient's condition was seemingly unchanged: the diarrhea persisted and a seclusion type of personality had developed. However, 4 of the patients who stated that they had made good progress mentioned having three to six loose bowel movements daily. The length of time since surgical interference was more than one year in 9 instances; it was less than that in the remaining 5 cases of the group.

A study of the causes of death furnishes some very interesting information concerning the selection of operation. Four of the patients died after performance of a short-circuiting operation; in 3 of these cases the procedure was performed as the first stage of a two-stage operation; in the fourth case ileostomy was provided in an attempt to place a completely involved colon and ileum at rest and was intended only as a palliative measure. The 3 patients having ileocolostomy died from embolism, hemorrhage from the ulcerated portion of ileum left in situ, and failure to transect the ileum in which a fecal fistula was present, neces-

sitating subsequently a total exclusion operation, after which the patient died of obstruction. The fourth death was that of a boy for whom ileostomy had been performed. An inadequate resection had been carried out elsewhere (apparently a short segment of ileum had been removed and the remaining ileum had been anastomosed with the cecum which was very likely diseased). Furthermore, the involved mesentery and regional lymph nodes were only partially removed in order that the cecum and ascending colon might remain in situ. Recurrent symptoms of a fulminating character soon made themselves manifest and, when this patient came to the clinic less than a year after the resection, involvement had extended distal to the original site as far as the sigmoid flexure. Fifteen days postoperatively, death ensued from a combination of conditions: deficiency, anemia, toxemia, hemorrhage, and pyoderma gangraenosum.

Two patients died after anastomosis and resection were performed in two stages. Both had had inadequate treatment although according to the history the disease was extensive at least two years before they came to the clinic. One of these cases was that of a man, aged 30 years. After the inadequate resection, he was fairly well for one and one-half years. Recurrence or continuation of the disease resulted in involvement of the distal portion of ileum and of the ascending, transverse, and descending colon with perforation and with formation of an abscess. Ileosigmoidostomy was performed but the patient died thirty-six days postoperatively. The other death occurred nine months postoperatively and has been described previously. In this case, also, the colon was extensively involved.

The single death, three months after the one-stage procedure was carried out, apparently would have occurred regardless of the type of treatment employed. All of these deaths, except one, occurred among patients who were at either one or the other of the extremes of the age group for the disease; that is, they were either in their teens or were more than 50 years of age. It would seem that both the old and the young who have regional enteritis are particularly susceptible to the disease or are less prone to develop resistance and immunity to its progress than are those of middle age. It will be found also that three of the deaths occurred after recurrence or extension of the inflammatory process had taken place with involvement of a large part of the colon. If such an eventuality transpires, the outlook is always extremely grave and surgical intervention has been fruitless.

A résumé of the results from all types of surgical treatment shows that improvement occurred in 33 cases (including 1 in which exploration alone was performed), that improvement did not occur in 4 cases, that 5 surgical deaths took place, and that 1 death ensued three months postoperatively and another nine months postoperatively. Three of the deaths were definitely attributable to extension of the disease. The opera-

tive mortality rate based on the total number of cases was 11.5 per cent, but, if calculated on the basis of the number of operations, it was 8 per cent.

Postoperative care undoubtedly has much to offer toward decreasing mortality and morbidity among these extremely ill patients. Besides the usual symptomatic care accorded patients after operation, there are two phases of the condition of patients who have regional enteritis that are particularly worthy of consideration. First, severe deficiency in nutritional elements has occurred as a result of the inroads of the disease and for several days after operation nothing can be taken by mouth to replenish these deficient stores. The judicious use of crystalline vitamins in solutions intravenously, restoration of basic elements by intravenous administration of sodium chloride and calcium chloride, replacement of serum proteins and of hemoglobin by transfusions of blood, all have a place in properly selected cases. Secondly, measures for decompression of a diseased bowel or, better still, the prevention of distention, retention, and ileus have a prominent place in postoperative therapy. Transduodenal continuous aspiration (Paine and Wangensteen[31]) is instituted at the earliest sign of such an occurrence. A rectal tube is inserted at regular intervals to prevent excessive accumulation of colonic pressure. In the majority of the cases in which we have employed resection in one stage, a Witzel type of enterostomy made proximal to the anastomosis has been provided at the time of the radical procedure. Gentle suction (about 30 cm. siphonage pressure) is applied to the catheter in the same manner as to the Wangensteen duodenal tube. This in itself is usually sufficient to keep the bowel decompressed. Recently, the Boothby,[32] Lovelace,[33] Bulbulian[34] oxygen apparatus has provided a very valuable addition to our armamentarium. The value and mechanism of an intake of a high percentage of oxygen in decompression of the bowel was noted by Fine, Sears, and Banks[35] in 1935. With the development of an efficient, convenient, and cheap apparatus for administration of 90 to 95 per cent oxygen, the procedure is feasible clinically and is highly efficacious therapeutically.

SUMMARY

The subject of regional enteritis has been considered from a general historical standpoint. Specific data obtained from the study of forty-four proved cases of regional enteritis have been presented. A conjecture as to the role of a filtrable virus as a causative agent has been advanced. The occurrence of three cardinal features, that is, a mass in the right lower quadrant of the abdomen, the presence of chronic intestinal obstruction, and positive roentgenographic details, has been shown to be present either singly or in combination in 95 per cent of the cases reported in this series. Surgical procedures have been discussed in detail, also their probable relationship to recurrence and to fatalities. In the

consideration of postoperative care, emphasis has been placed on the necessity of directing attention toward the correction of nutritional deficiency and to keeping the intestine decompressed. The use of a high concentration of oxygen in the inspired air has been found efficacious for this latter purpose.

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Review of Recent Meetings

REPORT OF THE ELEVENTH MEETING OF THE INTERNATIONAL SURGICAL CONGRESS, BRUSSELS, BELGIUM, SEPT. 18-22, 1938

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HISTORICAL Belgium is the logical place for an international meeting. Just outside of Brussels is the field of Waterloo, and there are many reminders of the recent world struggle on every hand. The International Surgical Society began its eleventh meeting in the beautiful Senate Chamber of the Palace of the Nation where some fifty patriots were condemned to death by the enemy for being loyal to their country, among them Edith Cavell.

In spite of an international crisis hovering over Europe, for five days all reference to national and racial differences was laid aside, and surgeons of all nations, friendly or hostile, gave a united interest to many important surgical problems. It is not inappropriate to mention that the presiding officer of the Congress was America's own beloved **Professor Rudolph Matas** of New Orleans. With a world-wide reputation as a scientist, a courtly manner, and a mastery of many languages, he seemed to be made for the honored position. He addressed the meetings in French, with frequent side remarks to distinguished Fellows from Spain, South America, Italy, or Germany in their own tongue. International members, as well as Americans, paid homage to this great and learned American surgeon.

The scientific sessions were held at the Auditorium of the Faculty of Medicine, while operative clinics were held at Hospital Saint-Pierre and Hospital Brugmann in Brussels and at the Surgical Clinics of Louvain.

A symposium on the **Surgical Treatment of Hypertension** was the subject for the first day, and the following papers were presented:

M. N. Pende, Rome: **Introduction to the Problem of the Surgical Cure of Arterial Hypertension.**—The surgical treatment of essential hypertension was proposed by him for the first time in 1924 with the resection of the greater and lesser left splanchnic nerves. The operation was performed for the first time in Italy by Pieri, of Udine, in 1929 and by Durante, of Genoa, in 1930 with favorable results.

The experimental and clinic basis of the operation proposed by him in the treatment of arterial hypertension is due to some extent to the knowledge (to which he has contributed since 1903) of the action that the resection of the splanchnic nerve has in reducing the adrenalin secretion of the corresponding suprarenal gland; to some extent on the extensive vasodilator effect that even the resection of the greater and the lesser left splanchnic nerves only has on the abdominal vessels; to some extent finally on the probability that the resection of the splanchnic nerve abolishes hypertensive reflexes, especially in the vascular abdominal field.

The operation introduced by **Pende** must be strictly limited to the hypertension cases, especially in young adults before senility in whom careful clinic examina-

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tion proves the absence of renal insufficiency phenomena or advanced damage of the arteries and heart. The existence or the presence of morbid events, as of the brain, the retina, or the limbs (angiospasms and neurosis events of ischemic origin), are not contraindications to the left splanchnicotomy. Even a mild azotemia of 0.50 contraindicates the operation.

The operative technique is the operation by the lumbar way, extraperitoneally, without resection of the last rib, as has been suggested by Donati, Durante, Ciceri. Sometimes local anesthesia with novocain is sufficient, but in most cases general anesthesia is preferred. Until now the operation has not given any mortality; the recovery after the operation is fast.

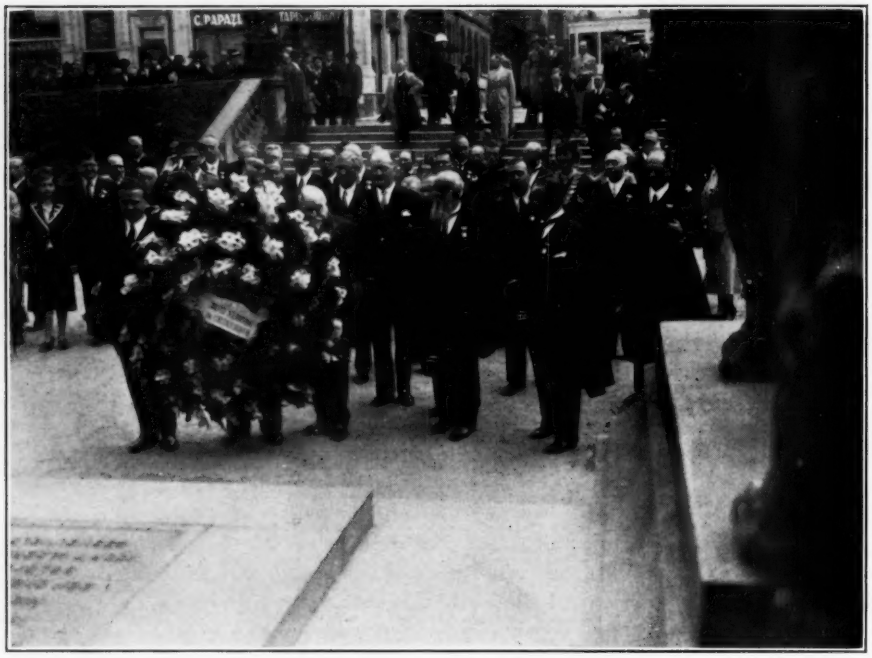

Fig. 1.—Dr. Rudolph Matas, President of the International Surgical Society, placing a floral wreath on the Unknown Soldier's grave. Brussels, Belgium, Sept. 19, 1938.

The day before the operation novocain anesthesia of the left splanchnic nerve should be done with Ciceri's technique. If this anesthesia does not cause falling of the blood pressure, even repeating the anesthesia two or more times, the operation is not indicated.

The operation must be limited to the resection of the greater and lesser splanchnic nerves, without other interventions on the sympathetic system or on the roots and on the suprarenal capsule. During the operation it is easy to discover the left suprarenal gland and to try to find suprarenal tumors. The experience of the cases operated in Italy with Pende's operation shows that we can have excellent results in very serious cases with the left splanchnicotomy only.

The analysis of the cases operated upon in which have been added to Pende's left splanchnicotomy the right splanchnicotomy or the partial surrenectomy unilateral or bilateral or ganglionectomies and rhizotomies, more or less wide, shows that his operation is not inferior to these others which are more complicated and more aggressive and which expose the patient to death in many cases.

M. P. Wertheimer, Lyons: **Arterial Hypertension: The Physiological and Pathological Problem From the Surgical Standpoint.**—Present-day theories on this subject show them to fall within three main groups; suprarenal, renal, and vasomotor. Surgical observations are related to these three theories and examined according to the way in which they seem to support one or the other of them.

Anatomic and pathologic considerations seem to lead to vascular and vasomotor explanations and are reinforced by the known facts of paroxysmal hypertension; while clinical observations incline one toward a renal theory, especially when the idea of nephroangiosclerosis is brought in. Experimental evidence favors new factors in permanent hypertension. Consideration of these new factors leads him to condemn any surgical intervention. Present-day knowledge of the problems involved does not justify an exclusive or systematic interpretation. He quotes two series of figures (those of M. Leriche and his own) which support the suprarenal theory, but he does not claim an absolute validity for these.

Mm. R. Alessandri and P. Valdoni, Rome: **Indications of Surgical Treatment and Clinical Results of Operations for Arterial Hypertension.**—The authors first of all deal with pathogenic considerations, because in the absence of any casual intervention these are precisely the ideas which serve to establish the directives for the various attempts at surgical treatment. The fundamental characteristic of the disease is represented by the increases in the systolic and diastolic pressures. The latter is the most interesting factor in isolating arterial hypertension as an autonomous disorder, independently of the variety of the pathogenetic mechanisms and complicating symptoms. Thus, arterial hypertension represents a disease with multiple pathogenesis.

The fundamental basis is the conception of a primarily functional disease and only secondarily organic. The increase in systolic pressure represents an adaption phenomenon and the increase in diastolic pressure the numerical expression of the increased peripheral resistance to the circulation. This increased resistance is the result of a spasm of the vascular wall. Sometimes the spasm is the result of renal disease, sometimes of a disturbance of the neuroendocrine regulatory mechanism of the circulation.

The authors emphasize the importance of certain etiologic coefficients, such as hereditary, constitutional and psychic factors, and the factors linked with certain hyperexcitable conditions of the sympathetic nervous system.

The cause of the spasm is due primarily to the constrictor action of adrenalin; this is demonstrated in certain cases of suprarenal tumors and by experimental work; the adrenalin acts when in excess or when present in normal quantities by the action of sensitizing substances, or by the action of synergic substances, and by a specific excitability of the vascular wall. In this last condition, the mesencephalic centers are important. Apart from adrenalin, the pituitary hormone is also important. In certain instances, a substance, not yet isolated but existent in the organism following changes in the renal parenchyma, may act in the same way as adrenalin. The first signs of the disease are confirmed in the region innervated by the splanchnic nerve, which plays an important role in vasoconstriction and in adrenalin secretion.

Apart from a pressure increase, the principal diagnostic signs are headache, exhaustion, and insomnia. During the first attack of essential hypertension, the prognosis is completely deceptive, and the disease begun in childhood is often discovered quite by chance while a measurement of the blood pressure is being made. The subsequent upward course is characteristic. After this first phase follows a period characterized by the appearance of organic cardiac, vascular, and renal lesions. The third phase, that of malignant hypertension, may also appear un-

expectedly. Frequently, when it is a primary occurrence, it is related to some renal disorder.

The authors then proceed to discuss the methods of differential diagnosis of paroxysmal hypertension, arteriosclerosis, renal sclerosis, and, in particular, the tests establishing the stage of the organic lesions and the importance of the functional disturbance.

Operative treatment is indicated when the organic changes are slight or lacking altogether, when medical treatment is of no avail, and when the disease is not secondary to a renal sclerosis. Surgical treatment in favorable cases may arrest the disease; in the majority of cases it can bring about a clinical recovery in patients by dispelling their subjective troubles, and in a smaller percentage of cases it may restore to normal level or may considerably reduce the increased blood pressure.

The results of surgical treatment available at present should induce practitioners of internal medicine to collaborate more actively with surgeons. Such a collaboration is desirable not only in the interests of the patient, but also because the investigation of clinical cases thus will become more complete; diagnosis, more exact; and the choice of subjects to operate upon, much easier. In short, judging from the results of surgical treatment, we can say that, with all the methods used and enumerated, a few favorable results have been obtained. That, in itself, is sufficient reason for surgeons to continue research and experiments, the more so as the good results obtained at present cannot be achieved by any other means. All surgeons seem agreed that the best results are obtained in essential juvenile forms, uncomplicated by arteriosclerosis or renal sclerosis; associations with diabetes, obesity, and menopausal disturbances do not appear to be of any importance. The application of the various operative methods is still in the experimental stage and, therefore, still dependent on personal choice rather than on any indication based on broad and definite comparative experience.

Sympathetic surgery is indicated only in cases free from vascular sclerosis, even though they are associated with diabetes, localized cerebral symptoms, and symptoms due to intracranial tumors, in which case it is sometimes necessary to carry out decompression trepanning. Selecting patients likely to benefit by operation is today a duty incumbent on the surgeon. Although there are several procedures, the authors give preference to alcoholization of the splanchnic. Alcoholization of the splanchnic may be indicated also in cases of sudden rise in tension, where it is necessary to lower the pressure rapidly. If there is a favorable result, it is made permanent by operation on the sympathetic. Splanchnic interruption is the fundamental stage of all the proposed modifications, but none of the modifications of Pende's operation present any real advantage for they are mere complications of a simple procedure without any sequel. Lumbar ganglionectomy is useless and injurious; resection of the anterior roots according to Alessandri and Valdoni, must be definitely rejected because of the heavy burden of abdominal muscular paralysis and the severity of the operation. In unilateral resection of the greater and lesser splanchnics, exploration of the suprarenal may be done, for it shows up the possible presence of a hyperplasia or tumor. At the same time, direct exploration of the kidney will permit of a more exact diagnosis of its pathologic condition. If, after such intervention, no good or adequate result is achieved, a second stage may be undertaken consisting of right splanchnic resection with total adrenalectomy.

Single stage operations on the adrenals are indicated in cases where one is led, by the presence of hypertensive crises, to suspect a suprarenal tumor or hyperplasia. What is important, especially in hyperplastic cases, is the presence of

suprarenal excess. Enervation and resection must be rejected because they are also valueless. Simultaneous exploration of the adrenals may be indicated when adrenalectomy has been decided upon.

M. M. Peet, Ann Arbor, Mich. (by invitation): **Surgical Treatment of Hypertension.**—Hypertension is a symptom of some constitutional disease manifesting itself in excessive activity of the sympathetic nervous system, probably due to some hormone from the adrenal or the kidney. We can symptomatically relieve it by denervating the abdominal viscera. This denervation can be accomplished easiest and safest by an approach to the sympathetic chains; i.e., the splanchic, major and minor, at the level of the eleventh rib, extrapleurally at the sites of the bodies of the vertebrae. Dr. Peet demonstrated this approach. The operation has the advantage of being less severe than others, making it possible for both sides to be denervated at the same time. He reported more than 300 patients operated upon, many with remarkably good results, others with indifferent results and some failures. After this experience he felt that the operation was justified in a great many patients and gave indications for the operation. He proposed to continue this procedure as long as it proved as useful as it apparently had during the past several years. This paper was well received by the Congress.

The foregoing papers were discussed by: **M. M. C. Heymans,** Ghent; **A. Chiasserini,** Rome; **R. dos Santos,** Lisbon; **A. Dickon-Wright,** London; **P. Cokkalis,** Athens; **E. Cutler,** Boston, Mass.; **C. Jeanneney,** Bordeaux; **J. Arce,** Buenos Aires; **W. Walters,** Rochester, Minn.; **A. Valerio,** Rio de Janeiro; **M. Donati,** Milan; **R. Fontaine,** Strasbourg; **Boghos Riad Ghali,** Cairo; **A. Jirasek,** Praha; **R. Appelmans,** Louvain; **M. Dogliotti,** Modena; **J. Bedrna,** Hradec Kralove; **A. Jentzer,** Geneva; **S. Cerqua,** Cairo; **S. de Dzierbowski,** Bydgoszcz; **E. Derom,** Ghent; **J. Strombeck,** Stockholm; **J. Jiano,** Bucharest; **J. Govaerts,** Brussels; **J. C. dos Santos,** Lisbon; **M. Hilarowicz,** Lwow; **M. Michon,** Paris.

The discussions embraced various phases of the question, some predicting further success with surgery, and others stating the opinion that the present surgical practices would be abandoned as of no benefit for hypertension. Other papers, of shorter duration, which were not on the official program, were read. The titles are as follows: **Dr. Ramon Palacio Posse,** Buenos Aires: **New Surgical Treatment of Mammary Ptosis; Dr. Bernard,** Giessen: **Anastomosis Between the Gall Bladder and the Intestinal Tract; Dr. H. Paschaud,** Lausanne: **Action of the Electromagnetic Waves in Operative Surgery; Dr. C. Daniel and Dr. Mavrodin,** Bucharest: **Treatment of Hypertension by Block Anesthesia; Dr. Klapp and Dr. Baumann,** Göttingen: **The Position of the Wire Extension in Repairing Fractures** (slides); **Dr. Reschke,** Griefswald: **The Manner of Handling Bleeding Tumors of the Stomach; Dr. Lexius,** Heidelberg: **The Artificial Blood Supply of the Kidney; Dr. Jaeger,** Munich: **The Method for Stomach Operations; Dr. Schorcher,** Munich: **A New Apparatus for Intravenous Blood Transfusion; Dr. A. Lob,** Munich: **Procedure in Stomach Operations; Dr. R. Gebhardt,** Hohenlychen-Mark: **Hohenlychener Film; Dr. L. Seiffert,** Neunkirchen: **Is It Possible to Totally Remove the Bladder Nowadays, and What Are the Conditions for a Successful Plastic Replacement of the Bladder?**

Symposium on Bone Grafts: M. B. Cuneo, Paris: **Introducing the Question of Bone Grafts.**—The method of bone grafting that gives the best results now is the autoplastic one, which can be used in various ways, the choice of which depends on the local conditions under which it will be used. The superiority of an autoplastic graft is of an hormonal nature, but the success of a graft depends essentially on the condition of the receiving bone. Osteoplastic grafts which possess

this hormonal power of stimulating bone formation on the surface of the receiving bone cannot exert their power unless the receptor is viable and shows the special activity itself. Autoplastic grafts are by far superior to homoplastic ones and still more so than heteroplastic material. It is better to use Orell's os purum than any nonautoplastic graft, but at the moment it is not possible to state definitely what is the osteogenic property of this os purum, save that it possesses it in a much less degree than does autoplastic material. It would perhaps be interesting to investigate the possibility of conferring an artificial osteogenic power on os purum.

The os novum formed by the tissues of the patient on whom the graft is proposed to be used can really be considered as an autoplastic graft of young bone. It seems to be an extremely interesting material, though its complicated technique must be borne in mind.

The age of the patient at operation is of prime importance, and the best results are obtained in children. There is a good chance of success in adults in good general health, as were the wounded of the last war. One must be much more reserved in considering patients who are more than fifty years of age.

M. Fr. Albert, Liege: **Biological Study of Bone Grafts.**—A collation of the vast literature and experimental work carried out in his laboratory has led Albert to the following conclusions:

Bone grafting is essentially a biological phenomenon, in which the essential role is played by the cells hereditarily adapted to bone formation. The superficial cells alone are capable of surviving and being grafted. The greater part of a bone graft is reabsorbed and replaced by new bone. For this replacement to take effect, however, the graft itself must furnish its own osteogenic cells, or else get them from the host on the spot (osseous stumps, site of fracture, or periosteum). Consequently, the living autogenous bone graft, partly covered over by periosteum, is always the ideal material. It alone can insure the success of a graft, when there is gross loss of osseous substance. The technique employed therefore should preserve to the full the unimpaired condition of the transplant cells and the vitality of the receptor tissues.

Dead bone may give favorable results, provided it has no antagonistic effects on the host tissues and can obtain from the host the osteogenic cells it lacks itself. The most practical type of dead bone is Orell's os purum.

For serious loss of bone substance or large interosseous space, os purum is an insufficient guarantee of success. In such cases, Orell himself has suggested the use of os novum, which he obtains by introducing dead bone chips under tibial periosteum. In this way the subperiosteal cells, which are intensely osteogenic, rapidly multiply, so that the young tissue invades the whole dead bone. Os novum is biologically equivalent to a living autoplastic graft and demonstrates in masterly fashion the very important role of the living osteogenic cell in rehabilitating and replacing the transplanted graft by new bone.

M. D. B. Phemister, Chicago: **Bone Transplantation in the Treatment of Tumors and Dystrophies of Bones.**—Relatively few bone sarcomas treated by resection and bone transplantation have been reported in the literature and in such cases local recurrence has been the rule. Tardiness in diagnosis is the chief obstacle to success. Five cases are reported. Two had local recurrences and metastases and died. Three were well 2⅓, 4½, and 7 years after operation. Benign tumors and bone cysts may usually be treated successfully by simpler methods not involving the use of the bone transplant. Advanced or complicated cases of benign giant cell tumor, solitary bone cyst, regional osteodystrophia fibrosa, Paget's disease, and fibroma of mandible calling for bone transplantation are recorded.

M. Bahld, Wurzburg (replacing Prof. M. Kappis, who died several weeks before the meeting): **Bone Transplants in Chronic Infections and Diseases of the Limbs.**—The value of bone grafting in chronic inflammatory conditions of the joints appears (1) in the formation of arthrodesis, (2) in rebuilding the rim of a joint cavity, and (3) in serving certain "biological ends."

Arthrodesis according to the methods of Albee and Hibbs, or other methods, is used in extremely varied conditions of the vertebral column. Five hundred cases are quoted from the literature of instances where sacroiliac arthrodesis was effected by the transplantation of pieces of bone; in this series 90 per cent of patients were either cured or greatly relieved. In the case of the hip, the transplantation of bone finds a use in arthrodesis, in building up a posterior buttress for the acetabulum, or in bone-pegging around the joint; the question of drilling the neck of the femur deserves investigation.

Bahld closed his paper with a discussion of the aims and methods of bone grafts considered in relation to the joints of the knee, the foot, the shoulder, the elbow, and the hand.

M. Sv. Orell, Stockholm: **Bone Grafts in the Treatment of Tuberculous Osteitis and Arthritis.**—The author reviewed the general literature on the use of bony grafts in the treatment of bone and joint tuberculosis after the extirpation of the focus and resection of the bones and joints and in athrodesis, particularly in spondylitis and tuberculous coxitis. The problem is surveyed in the light of the studies the author has previously conducted on the formation of new bone in experimental and clinical bone grafting which resulted in the introduction of two new forms of bone graft, called os purum and os novum. The former is dead bone which has been chemically and physically freed from fat, connective tissue, and protein; the latter is living, newly formed, soft, pliable bone which after subperiosteal implantation of os purum on the tibia has been obtained as a periosteal coating which after transplantation can more easily take up nutrition than can fresh live bone. The surgeon can thus perform bone grafting as previously with fresh autoplastic bone, compact or spongy, freely transplanted or pedunculated, or he can use os purum or os novum. Compact and spongy os purum can be stored up in the dry condition and sterilized immediately before using by boiling in physiologic NaCl solution. The different types of bony graft can be employed alone or in combination. It is advantageous to place a compact graft against compact bone and a spongy graft in order to obtain the best possible bony union. The surgeon is thus able to vary and combine the grafting material considerably, depending on the nature of each individual case, the location of the tuberculous focus, and the structure of the bed of the new graft.

With general hygienic dietetic therapy as the basis of the treatment, it is often possible to shorten the course of the cure after removal or healing of the tuberculous osteitis by doing a bone transplantation to secure new formation of bone or bony union, so that complete restitution or a firm bony union is obtained within the tuberculous region. The danger of recurrence especially after arthrodesis cannot be entirely eliminated, but the recurrence apparently can be better controlled than when these operations are not done.

Whether the transplanted bone has any influence on the tuberculous process itself is extremely difficult to decide definitely. It is obvious that the bone graft stimulates the tissues around to formation of new bone which goes on actively in the soft tissues in the bone canaliculi and on the surface of the bone. In this way the graft can speed up and ensure bone healing of the tuberculous focus. It also seems probable that the bony graft has a more general influence on the organism.

M. R. Demel, Wien, spoke on **Indications for a Free Introduction of a Piece of Bone in New Fractures and Pseudoarthritis.**

Harry Platt, Manchester: **Bone Grafting in Recent Fractures and Pseudarthrosis.**—(1) in recent fractures bone grafting is an ineffective method of securing internal fixation when compared with other forms of osteosynthesis such as plating. (2) The essential distinction between delayed union and true nonunion must be recognized. (3) Delayed union is a temporary suspension of osteogenesis which, in the majority of cases, can be successfully treated by conservative methods. Premature operative interference is to be condemned. In certain circumstances union may be hastened by drilling the fragments at the site of the fracture. Additional osteogenetic stimulus may be provided by a limited type of bone graft in the form of an osteoperiosteal, sliding, spongiosa, or peg graft. (4) In true nonunion a bone graft is required to act as a mechanical strut, as a conductor of bone, and as a producer of bone. The tibial graft best fulfills these requirements in pseudarthrosis of the long bones. (5) Two standard methods of insertion of the bone graft are of established value: (a) the inlay and (b) the onlay or massive graft. (6) In the compound injuries of civil life the two-stage operation used in the treatment of gunshot fractures is rarely necessary. (7) Failures after bone grafting are usually the result of technical faults, most of which are avoidable. The main causes of fracture are (a) infection, (b) inadequate contact between graft and host bone, and (c) insufficient immobilization. In a graft used to bridge a long gap, absorption or spontaneous fracture may occur in spite of an efficient technique. (8) The least favorable sites for successful grafting are the shaft of the femur, lower third of the tibia, and lower third of the humerus.

Papers on bone grafts were discussed by the following:

Mm. R. Alessandri, Rome; **O. Haberland,** Cologne; **Fr. de Quervain,** Berne; **R. Danis and F. Jonckheere,** Brussels; **J. de Fourmestraux,** Chartres; **D. Ferey,** Saint-Malo; **M. Zahradnicek,** Praha; **L. and F. Berard,** Lyons; **A. Lambotte,** Antwerp; **R. Fontaine,** Strasbourg; **R. Zanoli,** Pietraligure; **Fr. Cleret,** Chambery; **Gonzalez-Aguilar,** Barcelona.

Symposium on the Surgical Treatment of Cysts and Tumors of the Lung: M. F. Sauerbruch, Berlin, gave the introduction.

M. H. Constantini, Algiers: **Physiological Conditions of Pulmonary Surgery.**—Increased knowledge of the physiopathology of the pleuropulmonary system acquired during recent years has altered our methods and made possible new operations on the lung. Pneumothorax is generally tolerated well by vigorous and healthy young subjects. It is the shock of the collapse which calls out the vagosympathetic reflex capable of arresting the heart beat. The pulmonary elasticity, by allowing a sudden contraction, is responsible for these reflexes. Pressure anesthesia, today made possible thanks to the nitrous oxide apparatus and intratracheal anesthesia, counteracts the sudden collapse of the lung. Atropine, by paralyzing the vagus, and ephedrine, by stimulating the sympathetic, also mitigate the effects of collapse. The exposed lung easily chills and the patient therefore must be constantly warmed during operation. Bronchial effusions may be abundant and may obstruct the bronchial tubes, even to the point of asphyxia. The cough reflex, which evacuates them, therefore must be carefully maintained. The patient is operated on in the inclined position for the same reasons. Ligature of the hilar bronchus does not generally have any immediately serious consequences. Postoperative pneumothorax will eliminate sudden collapse reflexes, while oxygen therapy will eliminate asphyxia.

Pulmonary atelectasis, the usual cause of which is obliteration of the greater bronchi by thick mucus, may necessitate surgical intervention to free these bronchi. After pneumonectomy, the subject will be easily fatigued.

Exploratory thoracotomy, today without danger, may be of the greatest service in making possible an accurate diagnosis and the carrying through of that treatment which seems most suitable.

M. J. Arce, Buenos Aires: **Surgical Treatment of Cysts and Tumors of the Lung.**—The author states that the treatment of pulmonary cysts and tumors is essentially surgical. His report is divided into five sections. The first part deals with the preparation of the patient for operation. The second is concerned with what he calls the pleural risk; that is to say, the technical difficulties arising from artificial pneumothorax. He deals in a detailed manner with the methods and procedures for avoiding these difficulties. He pleads for preliminary pneumothorax, but also describes the indications for pressure anesthesia, artificial formation of adhesions, and surgical pneumothorax (Bazy, Delageniere, Duval). The author favors early exploratory thoracotomy and total pneumonectomy in tumors of the lung.

M. G. Forni, Venice: **Methods and Results of Operations for Pulmonary Tumors.**—Pulmonary tumors are generally bronchiogenic carcinomas; sarcomas and benign tumors are rare. Only 10 per cent of these tumors admit of radical treatment; i.e., pneumonectomy and lobectomy. Tumors of the greater bronchi and their main branches may be removed by total excision of the lung in one stage by the anterior route. Circumscribed peripheral tumors of bronchiolar origin are amenable to lobectomy by various techniques, either in two stages in a freed pleura preceded by pneumothorax and phrenic evulsion, or in two or more stages when spontaneous or artificial adhesions are present. Results of operation culled from collected operative statistics consist of 33 total pneumonectomies, 62 lobectomies, and 92 atypical operations. Of the 33 pneumonectomies performed, 30 were one-stage operations for carcinoma; 3 were in two stages for sarcoma. There were 10 recoveries, 3 lasting several years; the others, from a few months to 1 year; 3 deaths from recurrence and 20 postoperative deaths. Lobectomies (62) were performed 58 times for cancer (57 primary and 1 metastatic) and 4 for sarcoma (2 primary and 2 metatastic); 38 lobectomies were done in one stage, and of these 14 were successful, some of them for several years' duration. Eleven had fatal recurrences and 13 died after operation. Of 24 lobectomies in two or more stages, 9 recovered, 5 had recurrences, and 10 died at operation. The atypical operations were found to be inadequate and incomplete and revealed the highest mortality.

M. G. Baggio, Pisa: **Methods and Results of Operations for Pulmonary Cysts.**—Pulmonary cysts are either autochthonous or parasitic (echinococcal) in type. Lack of observations and the endemicity make it essential, in studying the results, to supplement the numerical with a critical element. Autochthonous cysts differ surgically from echinococcal cysts. Hydatid cysts may be cured spontaneously by emptying themselves into the bronchi, but this is a contingency one no longer waits for, and it has been replaced by suitable methods of surgical treatment. It is shown how dangerous it is to operate on a free pleura, because of certain influences, both direct and indirect, on the freely exposed pleura, influences which are not manifest in cases where the pleura is excluded. If the operation on the free pleura sometimes gives brilliant results, the operation on the excluded pleura and atelectatic lung offers more consistent ones, as for instance in pleural

plombierung. The simplest type of *plombierung* is that achieved by plugging with gauze. The author recommends following up the opening and evacuation of the cyst by superficial tubular drainage of short duration.

Autochthonous cysts do not lend themselves to a detailed critique, so far as results are concerned. In principle the cysts may be said to be susceptible to a mode of treatment similar to that used for echinococcal cysts. Multiple cysts necessitate lobectomy or pneumonectomy.

The following offered discussions: **Mm. T. Edwards**, London; **R. Alessandri**, Rome; **A. Young**, Glasgow; **S. Santy**, Lyons; **P. Cokkalis**, Athens; **C. Eggers**, New York, N. Y.; **A. A. Altounyan**, Alleppo; **S. de Dziembowski**, Bydhoszcz; **J. M. Mason**, Birmingham, Ala.; **R. Monod**, Paris; **Cl. Crafford**, Stockholm; **P. Wertheimer**, **M. Berard**, and **M. Dargent**, Lyons; **R. Chiarolanza**, Naples; **J. Divis**, Praha; **R. dos Santos**, Lisbon; **P. Valdoni**, Rome; **A. von Miorini**, Shanghai; **H. Paschoud**, Lausanne; **A. Trias-Pujol**, Barcelona; **G. Petrescu**, Ploesti; **Dervis Manizade**, Istanbul; **E. Lourat**, Bordeaux; **A. L. d'Arreu**, Cardill; **H. Fruchaud**, Angers; **G. Potoschnig**, Venice; **S. W. Harrington**, Rochester, Minn.; **M. Iselin**, Paris; **T. H. Sellors**, London; **M. Dargent**, Lyons; **Ch. Mayer**, Brussels.

REVIEW OF THE FORTY-SEVENTH FRENCH CONGRESS OF SURGERY, OCT. 17-22, 1938, PARIS*

ADOLPHE JUNG, M.D., STRASBOURG, FRANCE

(From the Faculty of Medicine and the Surgical Clinic of Professor René Leriche)

M. **CHARBONNEL** (Bordeaux) **and A. Sicard** (Paris): **Treatment of Recent Closed Fractures of the Spine.**—The first part of this report is devoted to the radiologic examination of the vertebral column, the authors emphasizing the necessity of performing this procedure in such a way as to reveal best the region involved.

M. Charbonnel: Treatment of Fractures of the Spine Without Nerve Complications.—

I. The four following methods are discussed: (1) Novocain infiltration (Leriche): Twenty to thirty cubic centimeters of 1 per cent novocain are injected bilaterally at a point opposite the lateral surfaces of the fractured vertebral body. The infiltration relieves vasomotor disturbances, ameliorates pain, and permits immediate active motion. (2) Functional method without reduction (Magnus): Absolute immobilization and reduction are not necessary. The patient is placed in the dorsal decubitus position for four weeks (without any attempt at reduction) and then active motion is encouraged. Two weeks later he is permitted to walk. (3) The functional method with reduction and plaster cast (Böhler): This method is modified after the procedure of reduction described by Davis (1929), Roger (1930), and especially Watson Jones (1931). Attention is directed to the fact that the principle of this treatment is the association of reduction and physical therapy. The well-known technique of Böhler, i.e., reduction in the ventral position, is described. After demonstrating that fractures in the dorsal region or above cannot be reduced in the ventral position, the dorsal decubitus position, commonly employed in France, is presented. The advantages of this latter method are that it is better tolerated and permits better reduction. The duration of immobilization varies from three to six months, depending upon the gravity of the case. Physical therapy must be used also. No serious nerve complication has been reported following this method of reduction. (4) Operative methods: Open reduction is justifiable only in the case of fracture dislocation with displacement of the articular facets in which combined hyperlordosis and continuous extension are not successful in reduction. The use of bone grafts (Albee, Halsted, Leriche) has been employed for immobilization either immediately after the occurrence of the fracture or later.

II. *Indications and Results of Treatment of Dorsolumbar Fractures (D^{11} to L^5).*—In fractures of the dorsolumbar area with slight displacement most authors consider attempted reduction unnecessary and advocate immobilization in the horizontal position for one to two months and the subsequent wearing of a light cast for several months. Others, however, prefer getting the patient up early, emphasizing the value of immediate active motion (Leriche uses repeated novocain infiltration for this purpose). Even in these cases, Böhler advocates reduction and application of a cast in hyperlordosis followed by physical therapy for six to seven weeks while wearing the cast. It should be added that other authors (De Beule and Schatte, and Constantini) have suggested prophylactic bone grafts even in slight fractures.

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The results of these various methods in slight fractures without displacement are good if the treatment is well applied and the patient is under constant surveillance. Permanent disability in cases in which the classical method (immobilization) is used is approximately between 10 and 20 per cent; whereas, in those treated by the Böhler method it is 0 to 10 per cent. Definite conclusions cannot be made regarding the treatment by novocain infiltration because of the insufficient number of cases but the results appear excellent.

In compression fractures of the dorsolumbar region the classical method of immobilization without reduction gives bad results in from 39 to 76 per cent of the cases. The method of Böhler seems to be of particular value in these cases because it has reduced these bad results to about 20 per cent. However, 30 per cent of the good results develop secondary compression. Early bone grafts without reduction give results which are better than those following the classical method and somewhat similar to those of Böhler. Early grafts after reduction and the use of physical therapy would appear the most advantageous, but the number of cases is too small to determine this. According to the author, early bony graft is formally indicated in: (1) comminuted fractures, (2) multiple fractures, (3) oblique fractures showing progressive displacement following reduction and application of plaster cast, and (4) fracture dislocations particularly with fracture of the posterior arch. It is also indicated in spondylolisthesis.

III. *Treatment of Dorsal Fractures (D^1 to D^{10}).*—The treatment used in fractures of the dorsolumbar region as described above is applicable also to fracture of this region. However, reduction in the dorsal position is more advantageous in this region. According to the author, the results obtained by the Böhler method (only 11.5 per cent bad results) are in contrast to those obtained by the classical method (43 per cent bad results). Considering the fact that secondary compression is particularly more frequent in dorsal fractures, early bone graft is indicated here, especially in fractures of several adjacent vertebrae.

IV. *Cervical Fractures (C^3 to C^7).*—In recent cervical fractures with displacement, most surgeons attempt reduction by constant traction (2 to 3 kg. of weight). This requires several hours or days and must be controlled by roentgenography, following which immobilization is obtained by a plaster cast.

The danger of secondary displacement is the most important consideration in the treatment of fractures of the cervical vertebrae. This is observed not only in unrecognized and untreated fractures but also in those in which reduction and application of cast have been done. Severe nerve complications may occur. (According to Soto-Hall, of 17 reduced cervical fractures there were 5 with secondary paralysis.) If reduction cannot be obtained, some authors advocate immobilization and bone graft when signs of secondary displacement appear. Others advise either immediate graft or after three to four weeks have elapsed. The author cannot make definite conclusions regarding the advisability of doing routine immediate bone grafts or doing grafts when displacement increases because in the two cases treated respectively in this way the late results were practically the same.

V. *Fractures of the Atlas and the Axis.*—These fractures are treated along the same principles as the preceding type of fractures. Reduction is obtained by constant traction. Bone graft is not performed routinely but done when a fracture-dislocation is insufficiently reduced or when secondary displacement occurs.

VI. *Multiple Fractures.*—In multiple fractures, occurring at different and distant levels, treatment consists of reduction in the dorsal position and in applying the support in the region of the most severe fracture. In cases of slight multiple fractures, therapy is functional with novocain infiltration.

VII. *In infants* under 6 years of age, treatment by classic immobilization with constant vigilance is sufficient. Prolonged surveillance is essential because certain

unrecognized and disfiguring fractures in young infants may be the origin of scoliosis appearing in adolescence. Children over 7 years of age may be treated in the same manner as adults, but bone grafts should be used very cautiously until the twentieth year.

A. Sicard: The Treatment of Fracture of the Spine With Nerve Complications.—

I. The author discusses first the anatomic, osseous, meningeal, and cord lesions, calling attention to the fact that marked osseous displacement does not necessarily indicate severe nerve lesions. Whereas extradural hematoma, being diffuse, does not usually produce compression of the cord, subdural hematoma, being localized, easily causes compression. One of three mechanisms may cause the development of a spinal cord syndrome: (1) vasomotor disturbances, (2) compression by fragment of bone or by hematoma, and (3) partial or total destruction of the spinal cord.

II. *The clinical manifestations* are not pathognomonic of each type of cord involvement. An incomplete paralytic syndrome, occasionally produced by slight cord involvement, almost always represents radicular lesions. On the other hand, in the presence of complete paralysis no clinical sign is pathognomonic of complete involvement of the cord. This can be determined subsequently with the rapid development of trophic changes, such as decubitus over the sacrum and heels and early and persistent priapism. Of the laboratory procedures, such as electric stimulation and lipiodol instillation and roentgenography, only the latter is important and of therapeutic significance in demonstrating the presence of a fragment of bone or an apophyseal articulation projecting into the spinal canal.

III. *The Methods of Treatment.*—(1) Absolute conservatism in addition to respiratory exercises and massage is advocated by some authors. The results are not convincing. Of 79 total paraplegias reported by Magnus, there were only 4 complete recoveries. (2) Reduction of the fracture which has certain advantages and is not dangerous except in the presence of impaction of the articular processes, in which case it is absolutely necessary first to release the impaction before attempting reduction in hyperlordosis. The role which reduction of the fracture may play in the development of cord lesions is considerable in certain cases. (3) Laminectomy which the author neither advocates nor discards routinely.

IV. *The Author Presents the Following Therapeutic Steps.*—(1) Do not remain inactive. (2) Orthopedic reduction except in severe shock, then (3) in partial paralysis, if pain persists after several days, laminectomy is advisable. (4) In complete paralysis, if spastic paraplegia is present (which is exceptional), reduction usually relieves the nerve involvement. If flaccid paralysis is present and no amelioration has occurred in one to two weeks, laminectomy should be done.

Discussion.—**Schotte** (Ghent) emphasizes the usefulness of epidural or paravertebral anesthesia in the treatment of nerve root disturbances following fractures of the spine. **Jacobovici** (Bucharest) reports personal observations. **Oltramare** (Geneva) discusses Kümmel-Verneiul syndrome which should be avoided by proper treatment. **Ch. Mayer** (Brussels), on the basis of 86 personal cases, is of the opinion that reduction has considerable advantages in simple fractures as well as in those with nerve complications. **Olgenick** (Amsterdam) emphasizes the importance of repeated lumbar punctures in certain cases. Edema, which may produce signs similar to anatomic section, causes only transient block of from eight to twelve days. If the block does not disappear, laminectomy is necessary. **Leriche** (Strasbourg) observes that, whereas it is generally agreed that immediate reduction should be done in cases of moderate severity, there is divergence of opinion as regards its value in the very severe cases. In benign cases and those in which reduction is contraindicated he uses novocain infiltration which has considerable advantages. In cases with nerve complications, unimproved after re-

duction, routine laminectomy is performed, preceded by cystostomy. **Lambotte** (Anvers) endorses the conclusions of Leriche as regards the efficacy of routine laminectomy in paraplegias. Laminectomy is never dangerous and an operative death has not occurred in 30 cases. Four cases saved by operation are presented briefly. **Fontaine** (Strasbourg) presents 7 cases with bone graft fixation in which the late results were excellent. In most of these the vertebral column is not ankylosed, is absolutely painless, and there is practically no disability. In cases of cord complications, he is in agreement with his chief, Professor Leriche, that laminectomy should be done almost routinely. Five of 11 operative cases were very much relieved, if not completely. **Jung** (Strasbourg) presents 3 cases treated by novocain infiltration in the clinic of his chief, Professor Leriche. The osseous lesion was slight in one case, the second case was a very old woman, and the third case was a very obese woman. These represent the three essential indications of novocain infiltration. The results are excellent. Attention is directed to his work with **Brunschwig** (Chicago) which showed the significance of the sensitive innervation of the articulation of the vertebral bodies. **Mallet-Guy** (Lyon) describes his technique of treating fractures of the spine. **Lambert** (Lille) states that he has obtained excellent results in 20 cases by reduction in hyperlordosis in the dorsal position, which he has employed since 1922. **Patel** (Lyon) emphasizes the fact that restoration of function is based on the anatomic lesion. **P. Wertheimer** (Lyon) calls attention to the usefulness of lipiodol instillation and the harmlessness of laminectomy. **Sénéchal** and **Hamel** (Paris) describe numerous techniques. **Delchef** (Brussels) selects the type of treatment most adaptable to the individual case. **Roeder** (Paris) calls attention to the difficulty of roentgenographic diagnosis in certain cases in which anomalies of the vertebrae may resemble fractures. **Chavannaz** (Bordeaux) emphasizes the frequency and severity of unrecognized fractures of the spine. **Grinda** (Nice) is of the opinion that the orthopedic treatment is efficacious and adequate in the majority of fractures of the spine. **Delageniere** (Le Mans) and **Arnaud** also took part in the discussion.

J. Patel (Paris) and **P. Moiroud** (Marseilles): **Clinical Forms and Surgical Treatment of Staphylococcic Septicemia.**—

J. Patel: I. *Clinical Aspects.*—The author describes the characteristic features of staphylococcic septicemia. The primary focus is usually in a wound or in a cutaneous infection, such as a furuncle. Other foci may be in the mucosal surfaces (angina or rhinitis), in puerperal or postportal infections, or in the genitourinary tract. Once septicemia exists, distant secondary foci are extremely frequent.

A. There are essentially two acute types of staphylococcic septicemia: (1) The type which appears as an acute infectious disease and the real diagnosis is determined only after the presence of staphylococci in the blood stream is established. Whereas in the fulminating form death occurs in three to five days, in the acute form the duration is from eight to twelve days. (2) The type in which the etiology is obvious. In this form the author considers the "malignant staphylococcic infections of the face" with secondary septicemia and the forms with early metastatic manifestations clinically appearing three to four days following the original infection. In those cases in which metastasis to bone (osteomyelitis) occurs or to the cutaneous region (purulent pustulous exanthemata) the infection can be attributed usually to the staphylococcic organisms.

Laboratory procedures demonstrating the existence of staphylococci in cutaneous pustules, in urine, and in blood establishes the definite diagnosis in these forms.

B. The subacute types are most common. After a period of frank septicemia, there is an apparent gradual subsidence towards recovery during which there appear evidences of localization most frequently in joints, bone, connective tissue, muscle, lung, and kidneys.

C. The chronic forms may be of embolic origin or follow an acute phase, of variable intensity, and sometimes of short duration. The metastatic manifestations may continue after the acute stage. Numerous and dispersed, these metastatic localizations occur in various sites, but are elective in the bones, the joints, and the connective tissue. They progress to abscess formation and the purulent contents constantly reveal the same type of staphylococci. Repeated blood cultures will demonstrate the existence of septicemia.

II. *Biologic Aspects of Staphylococcic Septicemia.*—The authors call attention to the fact that experimental staphylococcic septicemia in animals does not give the same pathologic manifestations that are observed clinically. However, it demonstrates certain facts: (a) that the route of propagation of infection is essentially venous, (b) that the infection may persist even after removal of the primary focus, and (c) that the staphylococci release a powerful and lytic toxin possessing lethal properties toward all the cells of the body, although by inoculation it can produce an active antitoxin.

In the circulation the staphylococci have a tendency to aggregate in contact with or in the interior of platelets or leucocytes. Whereas some are destroyed by this means, others, instead of being attacked, are actually protected. The organisms thus carried in the circulation may be eliminated in the bile, urine, and intestinal contents and in this process are apt to be altered (Fiessinger). Upon encountering the various elements of the reticuloendothelial system, the staphylococci produce destructive or necrosing and pyogenic lesions which are manifested in the following successive stages: microbic embolus, inflammatory reaction in the region of the thrombosed vessels, miliary abscess in the zone of infiltration. Aside from the cellular reaction, the staphylococci are destroyed by a humoral reaction (opsinins of Wright, stimulins of Metschnikoff, bacteriophage of F. D'Hérelle).

The author then concisely discusses the factors which cause a staphylococcic infection, such as a simple furuncle, accompanied by bacteremia as shown by positive blood culture but not a true septicemia, to be transformed suddenly under certain conditions into a true septicemia. Among these is the eventual toxicity to the organism and the development of virulence of the staphylococci which has long been considered but difficult to demonstrate. Other factors concern the biologic state of the host: intoxication, mistakes in therapy, avitaminosis, deficiency in hepatic and renal function, disturbance in sugar metabolism, and acidosis. The clinical behavior, the rarity of complete recovery, and the tendency to relapse of staphylococcic infections probably depend upon these fundamental factors.

P. Moiroud: The Treatment of Staphylococcus Septicemia.—The author states that, in spite of the primary clinical gravity of septicemia with diffuse suppurative localization, spontaneous recovery may occur unless there is involvement of the heart or brain. He considers the following types of therapy:

1. *Proper Means of Improving the General State.*—Transfusions, especially immunotransfusions, have given favorable results although difficult to evaluate. Shock therapy (using colloidal metals), which should not be employed in weak patients or those presenting myocardial disturbances or involvement, has had some success. Intravenous injections of carbon increases leucocytosis, stimulates the reticuloendothelial system, and seems to have an absorptive action on the toxin, but its practical efficacity is not certain. Vitamins, especially vitamin C, are particularly valuable.

2. *Treatment by the Products of Bacteria.*—Vaccinotherapy may be a double-edged weapon (Bazy). Useful in certain cases, in others it may stimulate the infection and increase its spread. The greater the virulence of the infection, the more attenuated the vaccine should be (Grégoire). Vaccinotherapy has been employed most in the osseous forms of staphylococcic septicemia. The results are impossible

to evaluate. The toxoids (Ramon) induce, in animals as well as in man, the formation of a specific antitoxin readily demonstrable in the serum. Aside from this, there exists in the serum a natural antitoxin of weak potency, produced by the staphylococcic infection. But it should be realized that a toxoid of high titer is not necessary for clinical recovery. Actually these investigations are in their incipiency and successes alternate with failures. The bacteriophage (d'Hérelle), according to certain authors, has a veritably heroic action. Sauvé employs it intravenously in desperate cases.

3. *Chemotherapy.*—The intravenous injections of mercurochrome (Young), acriflavine, and alcohol have had some success. Intra-arterial injections have been particularly efficacious in infections of an extremity. However, this does not displace local surgical therapy. Intracardiac injections (Leriche) of mercurochrome have been employed in two cases with transitory improvement. Intrafocal injections of antiseptics are of no value.

4. *Surgical Treatment.*—Surgical intervention, such as total excision of the atrium of infection, would appear logical, but it is more theoretical. It is impractical in malignant staphylococcic infections of the face. It may consist in certain cases of amputation of an extremity. But in most instances it is too late. Venous ligation, in an attempt to prevent the release of organisms into the general circulation, is valuable in certain cases but its practical usefulness is limited. Osseous localization must be considered seriously as regards therapy. The methods of intervention are incision, trephining, and resection. Early resection, known in France since Vigarous (Montpellier, 1761) and Ollier (Lyon, 1861), has been abandoned because of the danger of nonregeneration of bone. However, it has been applied recently with some success following the observation of Hallopean (1922). Subsequently Leveuf championed primary diaphyseal resection but at present he is more conservative.

In malignant staphylococcic infections of the face absolute conservatism is generally agreed upon. In cases of extension, ligation of the angular vein to prevent progression into the cavernous sinus has been advocated and performed but the majority of French surgeons, in contrast to their foreign colleagues, consider its advantages with considerable doubt.

Genitourinary localizations are the result of elimination of the micro-organisms by the kidney which occurs early and constantly. Perinephritic phlegmon, pyelonephritis, and prostatic abscess originate in this manner. The latter frequently opens spontaneously into the ureter, but surgical intervention may be necessary. Heitz-Bayer has approached these infections endoscopically. Subacute or chronic epididymitis, in certain cases, necessitates epididymectomy. The therapeutic indications in puerperal septicemia are very difficult to determine. Staphylococcic myositis is frequent especially in those cases in which vitamins B and C are lacking. Incision and resection are logical interventions. The author also calls attention to hepatic and pleuropulmonary localization, and to the occurrence of arterial emboli.

In conclusion the author emphasizes the usefulness of correlating all methods of therapy, the importance of not discarding general treatment, the revival of chemotherapy, and the present status of the delayed evacuation of metastatic collections.

Discussion.—**R. Debré** (Paris) calls attention to the definition of septicemia as conceived by Nicolle, which is based upon the presence of three factors: the presence of grave clinical manifestations indicating a severe infection, the existence of metastatic localizations, and the occurrence of numerous microorganisms in the blood. Bacteremias are frequent and occur especially in the terminal phase of malignant staphylococcic infections of the face and in osteomyelitis. Whereas these are not true septicemias, the borderline is not definitive. Whereas specific biologic

therapy may be employed with success in toxic diseases, it may not be valuable in diseases having a local virulent action. At present it is realized that the staphylococcus produces a toxin but staphylococcic infections are not essentially toxic diseases. Staphylococci may possess two pathogenic factors. From a surgical standpoint, respect should be shown the protecting wall surrounding a focus of infection. **J. Leveuf** (Paris) classifies osteomyelitis from a septicemic standpoint into two groups: (1) those in which blood cultures are positive in 57 per cent of the cases during the first two or three weeks (during this period intervention is contraindicated) and then become negative and the temperature drops; osseous changes become visible roentgenographically on the twelfth day; (2) those in which blood cultures remain positive and fever persists until death; these cases are true septicemia with osseous localization. **R. Leriche** (Strasbourg) states that the explanation for the development of septicemia on the basis of "increased virulence of staphylococci" is theoretical. Invasion of the microorganisms is actually due to lessened resistance of the host. Thus an infection which was previously latent or saprophytic may suddenly become pathogenic as a result of various excesses or exhaustion on the part of the host. Therapeutic investigations should be considered with this objective in mind. In this connection avitaminosis may be an important factor.

Others who took part in the discussion are: **L. Sauvé** (Paris), **Jeanneney** (Bordeaux), **F. Papin** (Bordeaux), **M. Vanlande** (Armée), **P. Lombard** (Algiers), **M. Arnaud** (Marseille), **L. Arnaud** (Saint-Etienne), and **P. Ulrich** (Paris).

P. Maulonguet (Paris) and **Pollosson** (Lyon): **Sarcoma of the Muscles and Connective Tissue of Extremities.**—This report is based on a study of malignant tumors of the extremities originating in muscle or in connective tissue which surrounds the muscles, nerves, and vessels. In this manner the authors include tumors of the soft parts and the vessels of the extremities as well as tumors having various histologic terms, such as myxoma, malignant lipoma, lipomatous myxoma, and rhabdomyoma. The term, tumors of the soft parts of extremities, is particularly bad, because from the present study there are excluded tumors of: connective tissue of skin, synovial bursae, lymphatic ganglia, nerves, and vessels. One hundred and nineteen cases of sarcoma of muscles and connective tissue of extremities were studied histologically and classified as follows:

(1) Sarcoma of mesenchymal cells	8
(2) Fibroblastic sarcoma	38
(3) Lipoblastic sarcoma	33
(4) Rhabdoblastic sarcoma	13
(5) Osteoblastic sarcoma	5
(6) Angioblastic sarcoma	16
(7) Giant cell sarcoma	6
(8) Superficial sarcoma (these are similar in character to the above types but originate superficial to the subcutaneous fascia and are relatively more benign)	10
(9) Myxofibrocytoma	7
(10) Xanthogranuloma	2

Careful anatomic study of these tumors reveals that they are apparently well encapsulated, including neighboring tissue as vessels, nerves, muscles, and bone only as adjacent structures. However, the connective tissue capsule does not necessarily indicate limitation of the growth. Leriche emphasizes the fact that neoplastic cells may be found in the connective tissue outside the capsule.

These tumors invade neither the vessels nor the nerves. Whereas sarcomatous cells infiltrate the periarterial tissue and the adventitia, they never extend to the

media of arteries. The vascularity of these tumors is usually very poor and according to the recent arteriographic studies of dos Santos the circulation of the tumors appears to be essentially venous. The lymphatics are almost always involved.

Sarcoma of muscles may be infiltrative or well encapsulated. It is important to realize that sarcoma of muscle as well as connective tissue can be osteoblastic and may be easily confused with tumors of osseous origin.

Metastasis is frequent and usually occurs in the pleuropulmonary region which was involved in 29 of the authors' cases. Certain benign connective tissue tumors, such as myxofibrocytomas, are difficult to distinguish even microscopically.

Clinically, sarcoma of the thigh occurs most frequently. It is usually well encapsulated, movable, not tender, and growing slowly. Functional disturbances as circulatory or nervous are remarkably absent for a long period of time. Adenopathy is also absent. Roentgenograms reveal the bone to be intact. Examination for distant metastasis, especially to the pleuropulmonary region, should be made.

The prognosis of these tumors is grave. They usually end fatally due to metastasis or after ulceration in the local area with secondary infection and cachexia. The prognosis is not good even in the treated cases. Of the 119 cases of the authors, 88 died, 15 recovered, and 16 are too recent to state results. Histologic study does not give definite significant information regarding the prognosis. Age is also of no prognostic significance.

Of the various methods of treatment, simple enucleation is to be condemned as recurrence practically always follows. Even total ablation is not satisfactory because it is too limited in scope. Amputation and disarticulation, except in late cases, are the only operative procedures which should be considered. The disarticulation should be either interscapulothoracic or interilioabdominal.

A considerable proportion of these tumors are radiosensitive. In a series of 45 cases the authors found 26 radioresistant and 19 radiosensitive. The histologic type determines this to some extent. Whereas certain forms of angioblastic and lipoblastic sarcomas are particularly radiosensitive, osteoblastic sarcomas and those of mesenchymal origin are radioresistant. Superficial sarcomas are less grave than the deep forms.

The authors report 15 total recoveries in their series of 119 cases. In addition to this there were 10 cases of superficial sarcomas with 6 recoveries. Of the successful cases, 5 were treated by local operation (undoubtedly these were not very malignant), 2 by amputation, and 10 by combined surgery and irradiation.

The authors make the following conclusions: (1) Whereas in the case of a small tumor total extirpation should be done rather than biopsy, in large tumors biopsy may be done but the laboratory report should be hurried. (2) Irradiation should be considered before surgical intervention as some tumors are radiosensitive. Even if the tumor is radioresistant, the loss of a few days is not significant. (3) In a large number of cases it will be necessary to resort to interscapulothoracic or interilioabdominal disarticulation.

The following took part in the discussion and in general agreed with the conclusions of the authors: **Gordon Taylor** (London), **Louis Tixier** (Lyon), **J. Guyot** (Bordeaux), **A. Hamant** (Nancy), and **P. Ulrich** (Paris).

Book Reviews

Surgical Diseases of the Mouth and Jaws. By Earl C. Padgett. Cloth. Pp. 807, with 334 illustrations. Philadelphia, 1938, W. B. Saunders Company. $10.

This well-written book will appeal in particular to three types of practitioners, the general surgeon, the plastic surgeon, and the dental surgeon. The author has attempted to bridge the gap between the domains of dentistry and surgery. The scope of the book, however, is considerably wider than its title would indicate. Extensive discussions of the management of the lymphatic areas of the neck tributary to epidermoid carcinoma of the mouth and face, the principles and application of irradiation in the treatment of malignant neoplasms, inflammations and diseases of the salivary and lachrymal glands, neuralgias and motor derangements affecting the face, mouth, and jaws, and diseases involving the neck enhance the value of the book considerably.

The dentist will find information which will enable him to detect lesions of the mouth earlier and more accurately. The general surgeon will find a clear delineation of the principles of treatment of those conditions which at the present time are properly treated only by the practitioner trained in both dentistry and surgery, of which there are not many. The plastic surgeon will find detailed discussions of practically all of the problems of reconstructive surgery having to do with the mouth and face. This portion of the book is profusely illustrated with both photographs and diagrams.

In general it can be said that the book is written in a conservative and orthodox manner. On subjects about which there may be debate, both sides of the question are presented and although the author frequently expresses his own ideas the reader is usually left to form his own opinion. The experienced surgeon will undoubtedly regret that the author does not express his own opinions more freely.

This book with its excellent illustrations, bibliography, and index can be well recommended to both student and practitioner.

Bile; Its Toxicity and Relation to Disease. By O. H. Horrall. Cloth. Pp. 434. Chicago, 1938, The University of Chicago Press. $4.

The author has summarized in 281 pages an extensive literature concerning the action of bile in health and diseased conditions. The bibliography alone covers more than 100 additional pages and contains more than 2,000 references.

It is pointed out by the author that one of the deterrents to more rapid progress concerning knowledge of the behavior of bile acids is lack of a wholly satisfactory chemical test for their presence. The author stresses the relative nontoxicity of bile pigments and indicates that bile acids are the essential toxic element in bile when biliary retention occurs or when bile escapes into abnormal locations.

A number of pathologic states bearing upon the physiology of bile are discussed, such as the hemorrhagic dyscrasias of jaundice, hemorrhagic pancreatic necrosis, bile peritonitis, jaundice, and external biliary fistula. The author summarizes the avail-

able information upon these subjects. This reviewer had expected to find some mention of the work of Whipple and his associates, which indicates the great value of the feeding of bile to obviate bleeding in jaundice. The author feels that the toxic action of bile salts and the transudation of protein-containing fluid into the peritoneal cavity are the responsible lethal factors in bile peritonitis. He is inclined to regard the bacterial factor in bile peritonitis as relatively unimportant. Unfortunately a chapter on the relationship of the biliary constituents to cholecystitis or cholelithiasis is not included.

The volume is authoritative and modern; anyone wishing to orient himself in the general problem of the physiologic actions of bile will do well to make the acquaintance of this monograph.

Athletic Injuries. By Augustus Thorndike, Jr. Cloth. Pp. 208, with 104 illustrations. Philadelphia, 1938, Lea and Febiger. $3.

This little monograph detailing the experience of the author over a five-year period in dealing with athletic injuries of Harvard athletes is an interesting and informative contribution. The author deals systematically with sprains, strains, dislocations, and fractures. In no sense does this text essay to discuss completely all the medical aspects of the various injuries. So little is known concerning the actual pathology of sprains and strains, that it would have been quite in order for the author, whose experience with them has been considerable, to debate upon them at length. He relates the experience of Leriche who exposed twice the tibiotarsal ligaments for sprain and found them intact; in consequence of this experience, Leriche believed that the disability of many so-called sprains was due largely to pain in the tissues about the tendons and came to inject novocain locally for relief of pain and loss of function. Whereas the author lends no factual proof, it is his belief that most sprains and strains are due to actual tears or ruptures of ligaments or muscle fibers. It is somewhat startling to learn that the author has employed the application of cold to the extent that phlebitis is a not uncommon accompaniment.

The author describes the physiology of exercise concisely and discusses, somewhat more briefly than the importance of the subject, the principles of therapy. A useful bibliography is appended. Surgeons who deal with athletic injuries and the minor accidents of industry will find this monograph useful.

The Operations of Surgery. By R. P. Rowlands and Philip Turner. Ed. 8. Cloth. Vol. I, pp. 1045, with 435 illustrations, 38 in color; Vol. II, pp. 998, with 514 illustrations, 4 in color. Baltimore, 1938, William Wood and Company. $10 per volume.

A ten-year interval has elapsed since the appearance of the seventh edition of this well-known two-volume text on operative surgery. In the meanwhile a new publisher sponsors its appearance in the United States and the senior author has died. In 1889 W. H. A. Jacobson, of Guy's Hospital, a surgeon of great learning, introduced the work as a single volume. It proved at once a tremendous success and from that day to this, this life-work of Jacobson has been appreciated everywhere and has enjoyed a great prestige and wide usage among English-speaking surgeons. Dr. Wm. J. Mayo is said to have remarked that two books were constant companions and guides in the early days of his surgical

career. One of these was Jacobson's *Operations of Surgery;* the other, Gerster's book on antiseptic principles of surgery. Kocher's *Operative Surgery* and Jacobson's *Operations of Surgery* have probably held a larger reading audience among English and American surgeons than any other similar books during their time. With the death of Professor Kocher in 1917, his work went out of print. Jacobson's work has been continued under the able directorship of successors at Guy's Hospital.

The general plan and format of the most recent edition of these two volumes follows closely that of the last publication. Some material has been added and some has been deleted. Only volume two on the abdomen has increased slightly in size. Ogilvie, Massie, A. Ralph Thompson, Gibberd, and R. C. Brock have revised and rewritten chapters in this new work.

One of the distinctive features of these volumes, the plan which is followed also in the eighth edition, is an adequate discussion of indications for operation, the choice of operative procedure, and the results both early and late of operation. In addition, pertinent references to literature are subtended at the bottom of the page. The illustrations in the main are quite satisfactory.

There is a wealth of information and experience summarized in these two volumes and any surgeon unfamiliar with them will do well to make their acquaintance.

More and more, however, it would appear that surgery in its manifold ramifications has become so broad that the writing of a complete work on operative surgery must of necessity become the task of a group of workers. When men write from their own experience, surgical barnacles drop out of texts of operative surgery and that which is best survives. One looks in vain through the text for information on some of the newer developments in surgery without satisfaction. Chapter 32 in volume two proposes to discuss some of the new things in surgery, but it is a poor and incomplete effort. This reviewer feels that if Jacobson's *Operations of Surgery* is to continue to enjoy the prestige which it has had for decades, subsequent editions must have more collaborators writing upon the field of their special interests.

The Synovial Membrane and the Synovial Fluid. By David H. Kling. Cloth. Pp. 299, with 80 illustrations and 34 tables. Los Angeles, 1938, The Medical Press. $5.

This little monograph deals with the anatomy and physiology of the synovial membrane and the state of the synovial fluid in joints in health and disease. It contains a large volume of information garnered from a number of sources. Practical chapters on the bacteriology of joint effusions, the technique of aspiration of joints and the injection of air into joints for purposes of diagnosis are included.

The author points out that the synovial fluid has normally a pH between 8.2 and 8.4, that it is in fact, next to pancreatic juice, the most alkaline fluid in the body. He also cites the susceptibility of articular cartilage to destruction with weak acid solutions. The capacity of the normal joint for absorption through the medium of the synovial membrane is pointed out.

The volume contains a great deal of useful information and needs to be read and studied to be appreciated. It can be recommended with enthusiasm to all those who have an interest in the physiologic behavior of joints.

Adventures in Respiration: Modes of Asphyxiation and Methods of Resuscitation. By Yandell Henderson. Cloth. Pp. 316, with 15 illustrations. Baltimore, 1938, Williams and Wilkins Company. $3.

The author has summarized in this monograph his ideas concerning the role of carbon dioxide in the control of respiration, asphyxia, and resuscitation of the newborn. Carbon monoxide asphyxia, mountain sickness, and acclimatization receive special consideration. The author believes that muscle tonus is a significant factor in initiating respiration at birth. Atelectasis accompanying operation, the author feels, is due in large measure to the depression of muscle tonus and particularly of the diaphragm which attends the administration of anesthesia.

There is much to commend in this volume and the surgeon, anesthetist, and obstetrician will find in it much useful information which he can apply practically.

The Surgery of Oral and Facial Diseases and Malformations. Their Diagnosis and Treatment Including Plastic Surgical Reconstruction. By George V. I. Brown. Ed. 4, cloth. Pp. 778, with 1019 illustrations. Philadelphia, 1938, Lea and Febiger. $10.00.

It may be said that there is a wealth of material in this book, so much so that a fair critical review hardly can be given. The feast of information begins with anesthesia in the first chapter, going through pathologic dentition, and includes a chapter on diseases of the nervous system of 113 pages with a color plate of photomicrographs of the gasserian ganglion. There are twenty-five chapters in all, with several on plastic surgery in the concluding pages that are more condensed. There are twelve color plates and many illustrations that are very good and clear. Some, however, are so small that the details cannot be made out. In the illustration of temporal muscle repair of a paralyzed face, the paralysis is shown on one side and the operative diagram on the other, which might prove misleading to some readers.

The statement is made that free skin grafts taken from another person will be satisfactory if both persons are of the same blood group. The fallacy of this, as far as our present knowledge of blood groups extends, is almost universally known, and, although it may have been an oversight, it is of enough fundamental importance to be somewhat unfortunate in a standard reference work.

In the preface the author indicates a wide range of readers to whom the book should prove valuable, and certainly it should to those who have worked with the author for it is a full summary of a long experience in this field of surgery.